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PREOPERATIVE RISK-ASSESSMENT METHODS, SHORT-TERM OUTCOME, AND PATIENT SATISFACTION IN ELECTIVE CRANIAL NEUROSURGERY

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ACADEMIC DISSERTATION

To be presented with the permission of the Medical Faculty of
the University of Helsinki, for public examination in the auditorium of
Peijas Hospital, Sairaalakatu 1,
on January 9th 2016, at 10 am.

HELSINKI 2015

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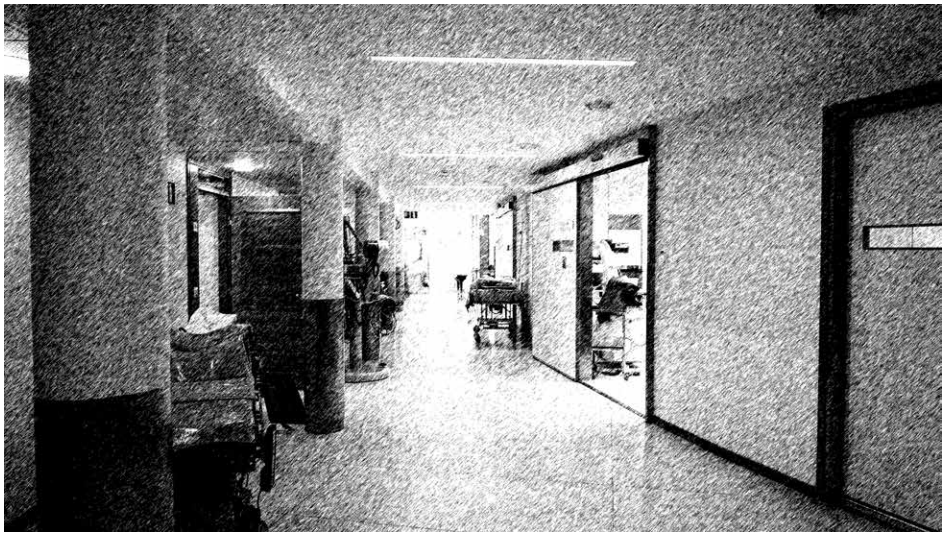
Dissertationes Scholae Doctoralis Ad Sanitatem Investigandam
Universitatis Helsinkiensis
ISBN 978-951-51-1756-4 (paperback)
ISSN 2342-3161 (print)
ISBN 978-951-51-1757-1 (PDF)
ISSN 2342-317X (online)

http://ethesis.helsinki.fi
Grano Oy
Jyväskylä, 2015
Finland



To Pade, Emil and Joel

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LIST OF ORIGINAL PUBLICATIONS

This thesis is based on the following original publications. In the text they are referred to by their Roman numerals (I-V). Articles have been reprinted with the kind permission of their copyright holders. In addition, this thesis presents some unpublished results.

I Reponen E, Tuominen H, Korja M. Evidence for the use of preoperative risk assessment scores in elective cranial neurosurgery: a systematic review of the literature. *Anesthesia & Analgesia* 2014;119(2):420-32.

II Reponen E, Korja M, Niemi T, Silvasti-Lundell M, Hernesniemi J, Tuominen H. Preoperative identification of neurosurgery patients with a high risk of in-hospital complications –a prospective cohort of 418 consecutive elective craniotomy patients. *Journal of Neurosurgery* 2015;123(3):594-604.

III Reponen E, Tuominen H, Hernesniemi J, Korja M. Modified Rankin Scale is a widely used but unreliable outcome measure in cranial neurosurgery - a prospective and unselected cohort study. Submitted.

IV Reponen E, Tuominen H, Hernesniemi J, Korja M. Patient satisfaction and short-term outcome in elective cranial neurosurgery. *Neurosurgery* 2015;77(5):769-776.

V Reponen E, Tuominen H, Hernesniemi J, Korja M. Patient-reported outcomes in elective cranial neurosurgery. *World Neurosurgery*. Published online ahead of print August 14, 2015.

ABBREVIATIONS

AANS	American Association of Neurological Surgeons
ACS	American College of Surgeons
AMI	acute myocardial infarction
ANOVA	analysis of variance
aPTT	activated partial thromboplastin time
ASA	American Society of Anesthesiologists
AUC	area under the curve
AV	atrioventricular
BMI	Body Mass Index
CAD	coronary artery disease
CI	confidence interval
CNS	central nervous system
COPD	chronic obstructive pulmonary disease
CPT	Current Procedural Terminology
Crea	creatinine
CRP	C-reactive protein
CRT	craniotomy
CSF	cerebrospinal fluid
DBP	diastolic blood pressure
DVT	deep venous thromboembolism
ECOG	Eastern Cooperative Oncology Group
EI	endovascular intervention
EUROHIS-QOL	European Health Interview Survey –Quality of Life
EuroSCORE	European System for Cardiac Operative Risk Evaluation
Gluc	blood glucose
Hb	hemoglobin
HR	heart rate
IBM®	International Business Machines
ICP	intracranial pressure
ICU	intensive care unit
K	potassium
KPS	Karnofsky Performance Score
LMWH	low molecular weight heparin
LOS	length of stay
Mac OS®	Macintosh Operating System
MCH	mean cell hemoglobin
MCHC	mean cell hemoglobin concentration

MCV	mean cell volume
MET	metabolic equivalent
MMSE	Mini-Mental State Examination
MRI	magnetic resonance imaging
mRS	modified Rankin Scale
MS®	Microsoft
Na	sodium
NICE	National Institute for Health and Care Excellence
NPV	negative predictive value
N2QOD	National Neurosurgery Quality and Outcomes Database
NSQIP	National Surgical Quality Improvement Program
OR	odds ratio/operating room
PCOR	Patient-Centered Outcomes Research
PE	pulmonary embolism
PMI	perioperative myocardial infarction
PONV	postoperative nausea and vomiting
POSSUM	Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity
P-POSSUM	Portsmouth Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity
PPV	positive predictive value
PREM	Patient-Reported Experience Measure
PRO	Patient-Reported Outcome
PROM	Patient-Reported Outcome Measure
PT	plasma prothrombin time
QOL	quality of life
RCT	randomized controlled trial
ROC	receiver operating characteristics
SBP	systolic blood pressure
SD	standard deviation
SKALE	Sex, Karnofsky, ASA, Location, and Edema score
SPSS®	Software Package for Statistics and Simulation
SVD	subjective visual disturbances
TYM	Test Your Memory
UTI	urinary tract infection
WI	wound infection
WHODAS-12	World Health Organization Disability Assessment Schedule 12-item version
WPW	Wolff-Parkinson-White

ABSTRACT

Aims

One objective of this study was to systematically review the current literature as to the use of preoperative risk-assessment scores in elective cranial neurosurgery. Other objectives were to study preoperative variables and scores in predicting short-term outcome, the reliability of the modified Rankin Scale (mRS) and of patient-reported outcomes (PROs) in short-term outcome reporting, and to study patient satisfaction in, to our knowledge, the first-ever unselected, prospective cohort of adult elective craniotomy patients.

Patients and Methods

First, we performed a systematic review of 25 studies on five preoperative scores [The American Society of Anesthesiologists' physical status classification (ASA) score, the Karnofsky Performance Score (KPS), the modified Rankin Scale (mRS), the Sex, Karnofsky, ASA, Location, and Edema (SKALE) score, and the Charlson comorbidity score] in predicting outcome in elective cranial neurosurgery.

We enrolled a prospective, unselected cohort of 418 adult elective craniotomy patients in the Department of Neurosurgery, Helsinki University Hospital. Evaluation of routinely collected preoperative data, original ASA score, Helsinki ASA score, and their combinations revealed their ability to predict in-hospital new central nervous system (CNS) deficits as well as systemic and infectious complications after elective craniotomy. Furthermore, we evaluated the reliability and accuracy of patient-reported outcomes, postoperative mRS scores, and mRS-score differences in reflecting short-term outcome. Overall patient satisfaction rate was determined, as were associations between high or low patient satisfaction and short-term postoperative outcome.

Results

Evidence as to the applicability of preoperative risk-assessment scores in elective cranial neurosurgery is scarce, with KPS receiving the most support in the literature. However, both ASA score and Charlson comorbidity score received support for risk stratification in selected patient cohorts. Furthermore, none of the scores predicted all postoperative outcomes; the most applicable risk score varied with the outcome measure selected.

The in-hospital mortality rate was 1.0% and the 30-day rate was 2.4%. In-hospital systemic and infectious complications occurred in 6.7% of patients, and new CNS deficits in 11.2%. Advanced age, preoperatively elevated C-reactive protein (CRP) level, and high Helsinki ASA class were independent predictors of systemic and infectious complications. A combination of these variables identified one-fourth of the patients with systemic and infectious complications and was associated with prolonged intensive care unit (ICU) stay (p=0.018) and hospital stay (p=0.004).

The rate of overall complications was 46.4%, and the rate of major complications was 18.2%. Perioperative changes in mRS scores were inconsistent: among patients with no complications, the mRS score increased for 17.1% at hospital discharge and for 23.8% at 30 days. Moreover, 28.0% of patients with major complications showed no increase in mRS scores at hospital discharge. Associations between patient-reported postoperative subjective deterioration in functional status and both major and overall morbidity were significant. Furthermore, a simple unweighted composite score of PROs was more sensitive and specific than was 30-day dependent functional status (mRS score ≥3) in detecting both major and overall morbidity.

In our cohort, 93.8% rated their overall satisfaction as good or excellent. Even 9 of 10 patients with postoperative major morbidity rated their satisfaction as high. Low patient satisfaction was associated neither with major (p=0.054) nor with overall (p=0.215) morbidity.

Conclusions

Strong evidence supporting the use of any existing preoperative risk score in elective cranial neurosurgery is lacking. The Helsinki ASA score seems more suitable than the original ASA score for elective craniotomy patients, especially in combination with other preoperative risk predictors, but only for systemic and infectious complications. The rate of major complications in elective cranial neurosurgery was moderate or even low considering the average age, comorbidities and operated lesions of the patients in our unselected study cohort. The postoperative mRS score and mRS-score difference were unreliable outcome measures after elective craniotomy: the changes in mRS scores were inconsistent with regard to the presence or absence of complications. PROs seem to be promising tools for postoperative reporting of outcomes. Overall patient satisfaction in elective cranial neurosurgery was high, even in patients with complicated outcomes.

TIIVISTELMÄ

Tavoitteet

Tutkimuksen tavoitteena oli arvioida systemaattisen katsauksen avulla tutkimusnäyttöä leikkausta edeltävien riskinarviointiluokitusten käytöstä aivoleikkauspotilailla. Lisäksi tavoitteena oli tutkia leikkausta edeltävien muuttujien ja luokitusten soveltuvuutta lyhytaikaishoitotulosten ennustamiseen, modified Rankin Scalen (mRS) ja potilaan ilmoittamien hoitotulosten luotettavuutta lyhytaikaishoitotulosten mittaamisessa sekä potilastyytyväisyyttä ensimmäisessä aikuisista aivoleikkauspotilaista koostuvassa valikoimattomassa prospektiivisessa kohortissa.

Potilaat ja Menetelmät

Teimme systemaattisen katsauksen 25 tutkimuksen tuloksista koskien viiden luokituksen [American Society of Anesthesiologists' physical status classification (ASA) -luokitus, Karnofsky Performance Score (KPS) -luokitus, modified Rankin Scale (mRS) -luokitus, Sex, Karnofsky, ASA, Location, and Edema (SKALE) -luokitus ja Charlson comorbidity score -luokitus] käyttöä aivoleikkausta edeltävässä riskinarvioinnissa.

Keräsimme prospektiivisesti 418 suunniteltuun aivoleikkaukseen tulevaa aikuispotilasta Helsingin yliopistollisen keskussairaalan Neurokirurgian klinikassa. Tutkimuksessa arvioitiin leikkausta edeltävien rutiinimääritysten, ASA-luokituksen, Helsinki ASA -luokituksen ja yhdistelmämuuttujien soveltuvuutta keskushermostokomplikaatioiden sekä systeemi- ja infektiokomplikaatioiden ennustamiseen. Lisäksi selvitimme leikkauksen jälkeisten potilaan ilmoittamien hoitotulosten, mRS-luokitusten ja mRS-luokkien muutosten luotettavuutta ja tarkkuutta hoitotulosten mittaamisessa aivoleikkauspotilailla. Määritimme myös potilaiden kokonaistyytyväisyyden ja lyhytaikaishoitotulosten vaikutuksen tyytyväisyyteen.

Tulokset

Tieteellistä näyttöä riskinarviointiluokitusten käytöstä suunnitellussa aivokirurgiassa on vähän. KPS-luokituksen käyttöä tukevaa näyttöä on eniten, mutta myös ASA-luokitus ja Charlson comorbidity score voivat soveltua valikoitujen potilasryhmien leikkausta edeltävään arviointiin. Mikään luokituksista ei ennustanut kaikkia hoitotuloksia; ennustearviontiin parhaiten soveltuva luokitus vaihteli valitun hoitotuloksen mukaan.

Sairaalakuolleisuus oli 1,0 % ja 30 vuorokauden kuolleisuus 2,4 %. Systeemi- ja infektiokomplikaatioita esiintyi 6,7 % ja keskushermostokomplikaatioita 11,2 % potilaista. Korkea ikä, kohonnut C-reaktiivisen proteiinin (CRP) taso ja korkea Helsinki ASA -luokka olivat systeemi- ja infektiokomplikaatioiden itsenäisiä ennustetekijöitä. Yksi neljästä potilaasta jolla oli kaikki nämä ennustekijät sai systeemi-tai infektiokomplikaation ja tarvitsi pidempää tehohoitojaksoa (p=0.018) ja sairaalahoitoa (p=0.004).

Komplikaatioita esiintyi yhteensä 46,4 % ja merkittäviä komplikaatioita 18,2 % potilaista. Leikkauksenjälkeiset muutokset mRS-luokassa olivat epäjohdonmukaisia: mRS-luokka oli huonontunut kotiutumisvaiheessa 17,1 % ja 30 vuorokauden kohdalla 23,8 % potilaista, joilla ei todettu leikkauksen jälkeisiä komplikaatioita. Lisäksi mRS-luokan nousua ei todettu 28,0 % merkittäviä komplikaatioita saaneista potilaista. Potilaslähtöisesti ilmoitetun toimintakyvyn huononemisen yhteys sekä merkittävien että kokonais-komplikaatioiden kanssa oli tilastollisesti merkitsevä. Lisäksi yksikertainen, painottamaton potilaslähtöinen yhdistelmämuuttuja oli 30 vrk kohdalla herkempi ja tarkempi tunnistamaan sekä merkittäviä että kokonaiskomplikaatioita kuin mRS luokka ≥3.

Valtaosa (93,8 %) potilaista oli hyvin tai erittäin tyytyväisiä saamaansa hoitoon, samoin jopa yhdeksän kymmenestä merkittäviä komplikaatioita saaneista. Tyytymättömyys hoitoon ei liittynyt merkittäviin (p=0.054) tai kokonaiskomplikaatioihin (p=0.215).

Päätelmät

Vahva tieteellinen näyttö leikkausta edeltävien riskinarviointiluokitusten käytöstä elektiivisessä aivokirurgiassa puuttuu. Helsinki ASA -luokitus vaikuttaa soveltuvan paremmin aivokirurgisten potilaiden systeemi- ja infektiokomplikaatioiden riskin arviointiin kuin alkuperäinen ASA-luokitus, erityisesti yhdistettynä muihin leikkausta edeltäviin muuttujiin. Merkittäviä komplikaatioita on elektiivisessä aivokirurgiassa suhteellisen vähän huomioiden tutkimuspotilaiden ikä, sairaudet ja leikkausindikaatiot. Leikkauksenjälkeinen mRS-luokka tai mRS-luokan muutos kuvaa huonosti hoitotulosta: mRS-luokan muutokset olivat epäjohdonmukaisia suhteessa leikkauksenjälkeisiin komplikaatioihin. Potilaslähtöisesti ilmoitetut hoitotulokset ovat lupaavia tulevaisuuden hoitotulosmittareita. Kokonaispotilastyytyväisyys elektiivisessä aivokirurgiassa on korkea jopa merkittäviä komplikaatioita saaneilla potilailla.

1. INTRODUCTION

Modern neurosurgery emerged in the late 1800s propelled by three important inventions: general anesthesia, antisepsis, and the theory of cerebral localization.[1] The next hundred years witnessed a rapid development of both surgical and anesthesiological techniques and of knowledge contributing to the state-of-the-art mini-invasive microneurosurgery of today. The expanding possibilities of neurosurgical care have raised expectations of a good functional and even aesthetic outcome after elective cranial neurosurgery.

Intraoperative and postoperative morbidity plays an important role in determining quality of life and functional patient outcome and has a major impact on the overall cost-effectiveness of surgical treatment.[2-4] Elective cranial neurosurgery is among the surgical subspecialties generally considered major surgery due to the high-risk profile associated with the vital importance of the brain and its delicate location inside the cranium.

Preoperative risk-assessment scores are designed to help clinicians in anticipating a patient's preoperative surgical risks. Several preoperative scores and models predict surgical outcome,[5] but their widespread use has been limited due to their poor specificity and sensitivity. An optimal risk-assessment scale would be reliable, brief, straightforward, objective, specific, and sensitive.

The American Society of Anesthesiologists' (ASA) physical status classification score is, worldwide, a preoperative risk score, even though it was not originally developed for this purpose.[6-8] This score is a validated assessment score in predicting outcome after major abdominal surgery, renal cell carcinoma surgery, general and vascular surgery, and spinal surgery,[9-12] and it can also predict perioperative mortality in elective noncardiac surgery.[13] Furthermore, some surgical subspecialties have succeeded in designing their own predictive preoperative models. For example, the European System for Cardiac Operative Risk Evaluation (EuroSCORE) risk stratification system is standard in assessing risk for cardiac surgery patients.[14, 15] The ASA score has, in fact, never been validated in elective cranial neurosurgery, and no neurosurgery-specific preoperative risk-assessment scores exist.

Preoperative risk stratification and risk-assessment scores are necessary both for clinical and for administrative purposes. Such

scores enable benchmarking, describing the patient case-mix, and comparing various patient series as well as treatment facilities. Furthermore, these scores facilitate institutional quality control and resource allocation. Preoperative risk-assessment scores also provide objective information for patient-centered clinical decision making. An international consensus on outcome-reporting criteria is a prerequisite for developing accurate risk-assessment scores.

A common belief is that neurosurgical patients' preoperative physical status and comorbidities contribute to surgical outcome, but a reliable preoperative risk-assessment score is necessary to facilitate decision-making in cranial neurosurgery. The surgical outcome, however, should also be measured accurately and objectively. Currently, what the most influential studies in elective cranial neurosurgery use, as their outcome measure, is the modified Rankin Scale (mRS).[16-20] Like the ASA score, the mRS was developed for a completely different setting and has never been validated in neurosurgical patients. Reliable and objective risk assessment and outcome reporting are vital to optimizing resource allocation in neurosurgery, where the average patient age and the prevalence of age-related comorbidities is constantly increasing.[21, 22]

The current patient-centered focus of health care emphasizes the direct input and involvement of the patients in their own care. In concordance with this view, patient satisfaction ratings are increasingly collected and even used for public outcome reporting and quality-of-care comparisons.[23] Furthermore, measuring patient-reported outcomes (PROs) could promote openness and patient safety as well as minimize any subjectivity and inter-observer agreement issues associated with the conventional scoring systems.[24-32]

The basis of this research project was a systematic review of the literature on preoperative identification of craniotomy patients at high risk for unfavorable short-term surgical outcome. The aims of our prospective cohort study were to study the accuracy of preoperative risk-assessment methods, PROs and mRS as measures of surgical outcome, and also overall patient satisfaction in elective cranial neurosurgery.

2. REVIEW OF THE LITERATURE

2.1 Preoperative evaluation of elective craniotomy patients

2.1.1 Organization of preoperative evaluation

The organization of preoperative consultations varies considerably between countries and even within individual treatment centers. Most western neurosurgical centers arrange preoperative consultations with the operating surgeon and anesthesiologist as well as routine laboratory measurements and necessary radiological imaging studies. Some centers, aiming to optimize resource usage, have started preoperative clinics for outpatient consultations, whereas the more conventional approach is to arrange consultations with the surgeon and the anesthesiologist upon arrival in the hospital ward the day before scheduled surgery. During the last decade, the emergence of preoperative clinics has been catalyzed by the surge in same-day admissions. Quantifying the impact of arranging a preoperative clinic remains a challenge for researchers, but clearly, such clinics can facilitate patient flow and minimize last-minute cancellations.[33] In many centers, the preoperative evaluation of neurosurgical patients follows the general preoperative evaluation scheme or department protocol, but specific practice guidelines have recently appeared.[34]

2.1.2 Patient history

A treatment decision should always be based on assessment of the patient holistically. Health-care outcomes improve through paying attention to patient context.[35] Patient-centered shared decision-making integrates both evidence-based medicine and the individual patient's values and preferences.[36] In this process, patient history is a valuable tool for the surgeon in evaluating the general health status and current symptoms of the patient to determine which treatment options are justifiable in each individual case. History thus plays a crucial role even before the decision to operate.

Patient history is also the basis of all anesthesiological preoperative evaluations. Overall perioperative risk depends on the patient's cardiorespiratory fitness, risks associated with specific illnesses or

general health status, and risks associated with the planned surgical procedure. Estimating the patient's cardiovascular capacity in Metabolic Equivalents (MET) gives vital information as to perioperative risk for cardiovascular complications or even mortality.[37] A rough estimate can result from asking simple questions such as walking distance and ability to perform household chores.

Many clinicians believe that knowledge of the patient's chronic illnesses, medications, and treatments is imperative for efficient preoperative risk modification and a successful anesthesia plan. To minimize risk for perioperative adverse events, all chronic illnesses and health risks including endocrine dysfunction,[38] diabetes,[39, 40] neurologic diseases,[41] heart conditions,[42, 43] hypertension,[44, 45] hyperthyroidism,[46] renal failure,[47-50] cirrhosis,[51, 52] and alcohol abuse[53] should be preoperatively in optimal balance. Thus, questions should aim at identifying ill-balanced chronic conditions. For example, a history of crescendo angina pectoris or poor glycemic control in a diabetic patient should raise concern and possibly lead to further diagnostic and therapeutic interventions in an attempt to stabilize the underlying disease before proceeding with any scheduled elective surgery.[37, 54] Such interventions should always be carefully weighed against the possible risks associated with delaying any planned surgery.

Additionally, illnesses and conditions affecting the choice of anesthetics or anesthesiological methods need careful assessment to guide in selection of the safest anesthesia modality for each individual patient. Accurate information on current medications is a cornerstone of successful preoperative assessment, because planning the perioperative medication is an integral part of every preoperative consultation.

Information about previous surgeries and anesthetics provides valuable clues to possible problems such as difficult airway or postoperative nausea and vomiting (PONV). A preoperative health questionnaire helps in addressing these issues, and additional information is often available in hospital databases.

Few studies exist on the effect of preoperative chronic illnesses on postoperative outcome in the specific subgroup of neurosurgical patients. Elective cranial neurosurgery is considered major surgery, but results from studies with mixed patient groups undergoing major surgery may not be directly applicable. At the very least, unique aspects inherent in elective cranial neurosurgery demand customized preoperative evaluations. Special attention should be paid to the

intracranial process occurring. The location, nature, and size of the lesion may play a role in planning not only the surgery but also the anesthesia. Due to the complication profile associated with cranial neurosurgery, the risk for bleeding and thrombosis in patients on antiplatelet drugs or anticoagulants preoperatively should be noted. Discontinuation and re-introduction of such medications during the perioperative period demands careful planning. Furthermore, epilepsy may be a symptom of the intracranial process due to be resolved by surgery; although adequate preoperative antiepileptic medication is indicated, the cure is surgical.

2.1.3 Clinical evaluation

A meticulous clinical status is at the heart of preoperative surgical consultation. It enables the surgeon to gain information on functional deficits and symptoms relevant to the planned operation. It also provides the patient with the opportunity to bring forward any questions concerning treatment and outcome prognosis. The clinical evaluation is preferably conducted by the operating surgeon and serves for individual planning of the whole perioperative care process including surgical details such as positioning and approach.

A preoperative consultation with the anesthesiologist is a common routine for all patients undergoing major surgery, including elective craniotomy. Evidence as to the positive impact of such consultations on outcome is lacking, but the general view is that a clinical evaluation benefits both patient and anesthesiologist. The patient receives information that helps alleviate anxiety associated with the upcoming surgery, and any obscurities can be clarified.[55, 56] The anesthesiologist observes the patient's general health status, assesses the airway, and makes focused clinical status assessments if any concerns arise. In elective neurosurgery, neurological symptoms and deficits and clinical signs of elevated intracranial pressure (ICP) deserve special focus, as these may play a significant role in planning both the surgery and anesthetic.

Active individual encouragement to stop alcohol or substance abuse and cease smoking reduces perioperative risk, but for full benefit, the intervention should take place at least four weeks prior to the planned surgery, before the preoperative clinical consultation.[57-62]

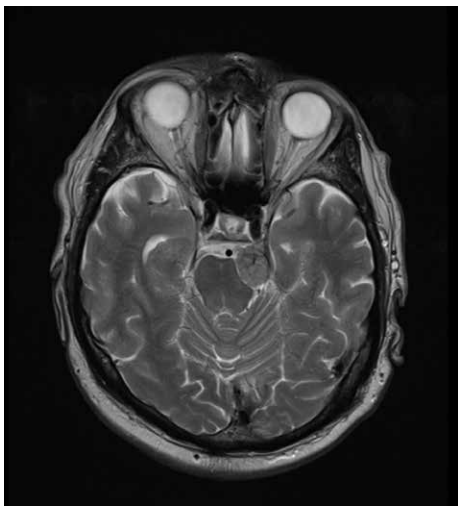
2.1.4 Laboratory measurements

In the absence of solid scientific evidence, the choice and extent of preoperative laboratory measurements is usually based on expert opinions such as the guidelines of the National Institute for Health and Care Excellence (NICE) or the American Society of Anesthesiologists (ASA).[63, 64] Screening tests are not a recommendation for healthy patients or patients whose chronic illness is in balance, especially preceding minor operations.[63, 65] Treatment centers have protocols regarding the range of preoperative laboratory tests in specific patient groups. For neurosurgical patients, preoperative laboratory tests identifying potential problems in blood coagulation or glycemic control (predisposition to infection) can be relevant to the complication profile. The value of routine prothrombin time measurements in elective neurosurgical patients with normal bleeding history is limited.[66] Furthermore, activated partial thromboplastin time (aPTT) may be more accurate in predicting postoperative bleeding.[67] All preoperative laboratory test choices should ideally be based on patient history, clinical findings, and risk factors associated with the planned surgery, and all sets of routine laboratory measurements should be complemented by further tests according to individual needs.

2.1.5 Radiological imaging

Awareness of the risks associated with radiation has reduced recommendations for routine chest x-ray studies; these should be considered only if clinical signs indicate a potential condition that can be treated or that can influence surgical outcome.[63]

Radiological imaging facilitates a successful neurosurgical operative plan. Besides the exact size, location, and nature of the lesion, also the disturbance of normal anatomy, signs of elevated ICP and abnormalities in the flow of cerebrospinal fluid (CSF) are detectable. For intracranial tumors, resonance imaging (MRI) is standard, but vascular lesions require angiography. Nowadays, conventional angiograms with x-ray are for the most part replaced by MRI angiograms with minimal radiation doses.



Extra-axial tumor compressing the brain stem.

2.2 Preoperative risk-prediction scores in surgery

2.2.1 Development of risk-prediction scores

Quantifying the risk involved in a surgical operation and anesthesia is a major clinical challenge. The need to communicate the perceived risk to other professionals and even to the patient has led to development of several risk scores. Some scores, such as the ASA Physical Status Classification score,[7] are general and applicable to large patient populations across surgical specialties. Other scores predict the risk in very specific patient subgroups, for example patients undergoing cardiac surgery, in an effort to improve the scores' sensitivity and specificity. Furthermore, some scores aim at predicting specific outcome events such as a perioperative myocardial infarction (PMI).[68, 69] Even scores originally developed for a completely different purpose have been adopted for preoperative risk assessment.[70, 71]

Generally, preoperative risk-assessment methods can be divided into two categories: risk scores and risk-prediction models.[72] Most of the widely used methods are risk scores unable to provide individualized prediction of risk for an unfavorable outcome.[73]

Developing a risk-prediction score requires large, methodologically impeccable clinical studies and complex statistical skills combined with a sound clinical understanding of the interrelations between preoperative variables and postoperative outcomes. The importance of correct and accurate definitions of variables, surgical procedures, and outcomes is emphasized in the development of risk-prediction scores for very narrow patient subgoups.[15]

2.2.2 Challenges of risk prediction scores and their implementation in clinical practice

Preoperative risk-prediction scores are useful supplemental tools for preoperative risk assessment; they cannot, however, replace the clinician's overall assessment and rarely incorporate a broader patient context. Risk scores have significant limitations of which the clinician should be aware.

Score validation, or the lack thereof, is important to recognize. A score well documented for one patient group may not be applicable or relevant for another. As with any treatment or medicine, sufficient evidence is necessary before implementing a risk prediction score

in clinical use for a specific patient group. Unfortunately, many risk scores have been generalized despite insufficient validation data.[7, 32, 71]

The complexity of a score is a double-edged sword: Simple scores[7, 32] are widely applicable, whereas complicated risk scores are more difficult to implement in everyday clinical work.[68, 74] However, the underlying reason for complexity is increased specificity and sensitivity, as well as the score's predictive value. Most often the score must be a compromise between these two conflicting interests.

Inter-observer consistency is another major challenge for many scores used for preoperative risk prediction. The ASA physical status classification and the modified Rankin Scale are both subject to this phenomenon, and many studies have addressed its effect on their reliability. [24-32]

Some scores are based on purely preoperative factors and objective findings.[7, 32, 68, 71, 75] Others, such as the Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM), incorporate intra- or perioperative data.

2.2.3 Example of customized risk prediction: The EuroScore

In an effort to improve the quality of cardiac surgical care, the European system for cardiac operative risk evaluation (EuroSCORE) database served as a source for developing the EuroSCORE risk-stratification system for prediction of early mortality in cardiac surgical patients.[14] The risk-score system, published in 1999, is based on objective risk factors for postoperative mortality. The reasons for developing such a specific risk stratification system included the need to couple mortality as an outcome with the risk profile of a hospital's case mix. This coupling provides a risk-assessment tool for patient-centered shared decision-making, and promotes openness and benchmarking between care facilities.

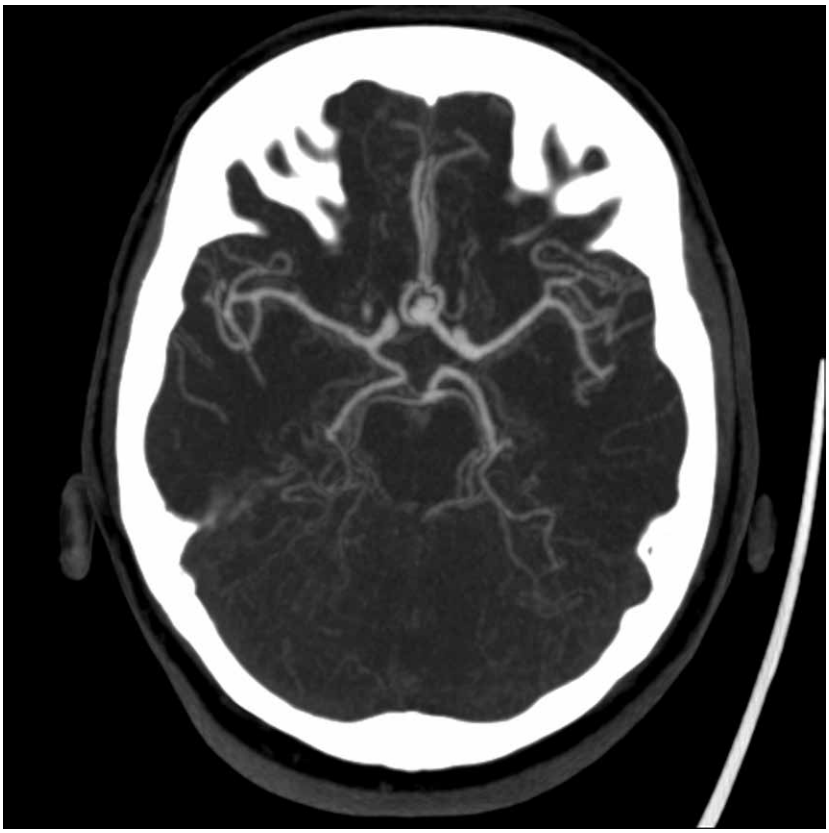
The original EuroSCORE is a complex scoring system with 19 patient- and operation-related factors and their weighted scores. The risk is categorized as low, medium, or high, and mortality increases from 0.8% in the low-risk group to 11.2% in the high-risk group.[14] EuroSCORE predictive performance was, however, rated poor in one systematic review.[76]

In 2012 an updated version (EuroSCORE II) replaced the original model. Its methodology was similar to that of the original score, but EuroSCORE II is derived from a more current dataset which reflects increased patient safety and decreased postoperative mortality.[15] A

subsequent update project, EuroSCORE III, is underway.[15] A recent meta-analysis confirms the performance of the EuroSCORE II model.[77]

Development of the EuroSCORE was possible due to a large database with up-to-date, complete, and accurate perioperative data on cardiac surgery patients across Europe. Patients in the original developmental subset numbered over 13,000, and the score was validated in a subset of almost 1,500.[14] The updated EuroSCORE II was derived from a dataset of almost 22,400 patients and validated in a subset of more than 5,500.

Despite its rather complex nature, the EuroSCORE has been widely and successfully implemented in clinical practice and even incorporated into hospital databases.



Computed tomography angiography showing the Circle of Willis and an anterior communicating artery aneurysm.

2.3 Proposed scales for preoperative evaluation of elective craniotomy patients

2.3.1 ASA Physical Status Classification

The ASA physical status classification was first introduced in the 1940's and revised in 1963,[6,7] and is probably the most widely known and used model of preoperative risk-assessment scores. The current ASA classification comprises six categories, ranging from healthy patients (ASA class 1) to severely ill patients likely to die within 24 hours without surgery (ASA class 5) and even to brain-dead organ donors (ASA class 6). The current ASA classification criteria are in Table 1. Since October 2014, ASA has provided examples to guide the clinical use of the classification.[8] The ASA physical status classification is a brief scale and easy to use in various clinical settings.

The ASA classification, despite its simplicity and familiarity among anesthesiologists, has received heavy criticism for its inter-rater variability and dependence on the subjective views of the attending clinician.[24-28] Furthermore, various modifications of the ASA classification exist. Their diversity causes difficulty or even makes it impossible to compare studies conducted in different institutions and countries. Along with the tremendous increase in standard of living since the ASA classification was first introduced has come a change in the prevalence and incidence of many illnesses. The classification itself, however, has remained virtually unchanged. The limitations of the classification underwent careful discussion in the original article by Saklad et al. in 1941.[7] Modern anesthesiologists seem to have forgotten that its original purpose was to describe the physical status of a patient with one classification for scientific and statistical purposes –not to assess the anesthesiological or operative risk associated with a surgical procedure. Regardless of these shortcomings and the lack of validation, the ASA classification is still in daily clinical use in neurosurgical units worldwide, both for intracranial tumor surgery,[75, 78-84] and for cerebrovascular surgery.[85]

Table 1. The American Society of Anesthesiologists' Physical Status Classification.7, 8

Description	ASA score
A normal healthy patient	1
A patient with mild systemic disease	2
A patient with severe systemic disease	3
A patient with severe systemic disease that is a constant threat to life	4
A moribund patient not expected to survive without the operation	5
A declared brain dead patient whose organs are being removed for donor purposes	6

ASA, American Society of Anesthesiologists.

Adapted from "Evidence for the Use of Preoperative Risk Assessment Scores in Elective Cranial Neurosurgery: A Systematic Review of the Literature" by Reponen et al., *Anesthesia & Analgesia* August 2014 - Volume 119 - Issue 2 - p 420-32 (Study I). Printed with permission from Wolters Kluwer Health Lippincott Williams & Wilkins©

2.3.2 Karnofsky Performance Score (KPS)

The KPS is originally a scale for the functional status of cancer patients.[71] It has also served for surgical risk prediction, especially in neurosurgery. The score ranges from 0 (deceased) to 100 (normal healthy person with no signs of illness)(Table 2). In intracranial tumor surgery, the KPS is one of the most popular preoperative risk scores.[86-89] In addition to patients with malignant tumors,[81, 83, 90-93] it is routinely applied to those with intracranial meningioma.[75, 78-80, 84, 94]

Table 2. Karnofsky Performance Score.[71]

Description	KPS score
Normal, no complaints, no evidence of disease	100
Able to carry on normal activity; minor signs or symptoms of disease	90
Normal activity with effort, some signs or symptoms of disease	80
Cares for self; unable to carry on normal activity or to do active work	70
Requires occasional assistance, but is able to care for most of his personal needs	60
Requires considerable assistance and frequent medical care	50
Disabled; requires special care and assistance	40
Severely disabled; hospital admission is indicated although death not imminent	30
Very sick; hospital admission necessary: active supportive treatment necessary	20
Moribund; fatal processes progressing rapidly	10
Dead	0

KPS, Karnofsky Performance Score

From "Evidence for the Use of Preoperative Risk Assessment Scores in Elective Cranial Neurosurgery: A Systematic Review of the Literature" by Reponen et al., *Anesthesia & Analgesia* August 2014 - Volume 119 - Issue 2 - p 420-32 (Study I). Printed with permission from Wolters Kluwer Health Lippincott Williams & Wilkins©

2.3.3 mRS score

In the 1950's, Dr. John Rankin developed a score for assessing the outcome of stroke patients.[70] This was later modified for the United Kingdom transient ischaemic attack (UK-TIA) aspirin study,[95] and the modified version was validated by Van Swieten et al. in 1988.[32] The mRS score ranges from 0 (no symptoms) to 6 (dead) (Table 3). At scores 0 to 2 patients are functionally independent, whereas at scores 3 and higher patients are dependent on other's aid in everyday activities. In cranial neurosurgery, the mRS often serves for preoperative risk prediction in cerebrovascular surgery patients.[96, 97]

Table 3. Modified Rankin Scale.[32, 70]

Description	mRS score
No symptoms	0
No significant disability. Able to carry out all usual activities, despite some symptoms	1
Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities	2
Moderate disability. Requires some help but able to walk unassisted	3
Moderately severe disability. Unable to attend to own bodily needs without assistance and unable to walk unassisted	4
Severe disability. Requires constant nursing care and attention, bedridden, incontinent	5
Dead	6

mRS, modified Rankin Scale.

From "Evidence for the Use of Preoperative Risk Assessment Scores in Elective Cranial Neurosurgery: A Systematic Review of the Literature" by Reponen et al., *Anesthesia & Analgesia* August 2014 - Volume 119 - Issue 2 - p 420-32 (Study I). Printed with permission from Wolters Kluwer Health Lippincott Williams & Wilkins©

2.3.4 Charlson comorbidity score

The Charlson Comorbidity Score is a weighted index that takes into account the severity of a patient's comorbidities. It was originally developed as a prospectively applicable method for classifying comorbid conditions which might alter the risk of mortality in longitudinal studies.[98] A total of 22 comorbidities are considered in this score, each one assigned a weighted score of 1, 2, 3, or 6. The sum of the scores represents the patient's overall comorbidity. The Charlson Comorbidity Index is a later version of the score in which every decade of age over 40 raises the total score by 1. In short, the higher the score, the higher the risk of adverse outcome after surgery. Weighted scores for

various comorbidities according to the Charlson comorbidity score are in Table 4. The Charlson comorbidity score has been applied in the preoperative risk stratification for patients with intracranial tumors[99, 100] and with unruptured intracranial aneurysms.[101]

Table 4. Charlson Comorbidity Score.[98]

Conditions	Score
Myocardial infraction (history, not ECG-changes only) Congestive heart failure Peripheral vascular disease (includes aortic aneurysm ≥6 cm) Cerebrovascular disease: CVA with mild or no residua or TIA Dementia Chronic pulmonary disease Peptic ulcer disease Mild liver disease (without portal hypertension, includes chronic hepatitis) Diabetes without end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes)	1
Hemiplegia Moderate or severe renal disease Tumor without metastases (exclude if >5 years from diagnosis) Leukemia (acute or chronic) Lymphoma	2
Moderate or severe liver disease	3
Metastatic solid tumor AIDS (not just HIV-positive)	6

For each decade >40 years of age, a score of 1 is added to the above score to yield the total Charlson Comorbidity Index score.
AIDS, acquired immunodeficiency syndrome; CVA, cerebrovascular disease; ECG, electrocardiogram; HIV, human immunodeficiency virus; TIA, transient ischemic attack.

From"Evidence for the Use of Preoperative Risk Assessment Scores in Elective Cranial Neurosurgery: A Systematic Review of the Literature" by Reponen et al., *Anesthesia & Analgesia* August 2014 - Volume 119 - Issue 2 - p 420-32 (Study I). Printed with permission from Wolters Kluwer Health Lippincott Williams & Wilkins©

2.3.5 SKALE score

A proposed risk-assessment system for meningioma patients called the Sex, Karnofsky, ASA, Location, and Edema (SKALE) score comprises five independent factors: sex, KPS, ASA classification, meningioma location, and peritumoral edema.[75] Each factor earns 0, 2, or 4 points, and a low total score suggests an unfavorable neurological outcome (Table 5). The SKALE score is applicable only to intracranial meningioma patients.[75, 84]

Table 5. The Sex, Karnofsky Performance Score, American Society of Anesthesiologists Class, Location of tumor, and Peritumoral Edema (SKALE) Grading System.75

	Score		
Factors	0	2	4
Sex	M	F	-
KPS	≤50	60-70	≥80
ASA class	IV	III	I or II
Location	Critical	Not critical	-
Edema	Severe	Moderate	No edema

ASA, American Society of Anesthesiologists; F, female; KPS, Karnofsky Performance Score; M, male.

From "Evidence for the Use of Preoperative Risk Assessment Scores in Elective Cranial Neurosurgery: A Systematic Review of the Literature" by Reponen et al., *Anesthesia & Analgesia* August 2014 - Volume 119 - Issue 2 - p 420-32 (Study I). Printed with permission from Wolters Kluwer Health Lippincott Williams & Wilkins©

2.3.6 Other scores

2.3.6.1 POSSUM and P-POSSUM

POSSUM and its modified version P-POSSUM (Portsmouth Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity) are complex risk-prediction models.[102, 103] A recent systematic review on risk stratification tools for noncardiac and nonneurological surgical patients supported the use of P-POSSUM for predicting morbidity and mortality.[72] POSSUM and P-POSSUM can provide individualized prognostic figures and have been applied to neurosurgical patients in a few studies, but require estimation of intraoperative factors such as blood loss. Due to their complexity, the POSSUM scores are not easily applicable in a clinical context and lack validation for use in cranial neurosurgery.

2.3.6.2 ECOG Performance Status

The Eastern Cooperative Oncology Group (ECOG) has published a performance status score with the aim of assessing how the patient's disease is progressing, assessing how the disease affects daily life, and determining appropriate treatment and prognosis.[104] It is a six-tier score in which zero represents a fully active and capable individual, three represents a patient dependent on the help of others, and 5 represents those deceased. This scale was originally developed for oncological patients, but has not been extensively applied to patients with brain tumors. Thus, its applicability to an unselected cohort of elective craniotomy patients remains unsupported by current evidence.

2.4 Scales measuring cognitive function

2.4.1 MMSE

The mini-mental state examination (MMSE) is the gold standard in assessing a patient's cognitive status and memory. Folstein et al. introduced the original test in 1975 with the aim to differentiate organic from functional psychiatric patients.[105] Comprising 30 questions, the test is relatively short and can be completed within the time constraints of a normal outpatient visit at a health-care center or hospital outpatient clinic. The questions in the MMSE involve knowledge of time and place, repetition of word lists, arithmetic, language use and comprehension and basic motor skills. The maximum score is 30, and any score ≥27 points indicates normal cognitive status. Cognitive impairment is categorized as severe (0-17) or mild (18-24 points). The MMSE is most valuable as a screening device or a diagnostic adjunct.

The major advantages of the MMSE include its validity and reliability for the diagnosis and longitudinal assessment of Alzheimer's disease, and its feasibility in clinical practice because of its ease of use and brevity. The test, however, has some considerable disadvantages, including its being affected by factors such as age or educational attainment. Physical problems, poor vision, and hearing loss can interfere with interpretation if not properly addressed. Furthermore, the MMSE lacks sensitivity to identify mild cognitive impairment and progressive changes occurring with severe Alzheimer's disease.

The MMSE test requires a trained administrator who observes the patient, asks the specified questions, records the answers, and finally, after the completion of the test, calculates the total score. Thus, the test cannot be filled in by the patient alone, and the use of the MMSE test in a study setting requires substantial personnel resourcing.

2.4.2 Test Your Memory (TYM)

The TYM tool was developed to fulfill three criteria that other cognitive tests fail to meet. It was designed to require minimal operator time to administer, to test a reasonable range of cognitive functions, and to be sensitive to mild Alzheimer's disease.[106]The time criterion was achieved by design of the test to be self-administered, unlike the MMSE, without any need for a trained administrator. Average time for test completion has been reported at 5 minutes.[106] The TYM

consists of 10 questions, and the maximum score is 50 points. In the original validation study, a TYM score ≤44 points detected 96% of patients with mild Alzheimer's, and a score of 45 points or higher thus implies normal cognitive status.

The TYM may have several advantages over other tests of cognitive dysfunction. It is brief, yet not too limited for grading the severity of any cognitive impairment. The reasonably wide range of scores in the TYM test allows for better discrimination and improves its suitability for monitoring. Inter-rater agreement for scoring is excellent due to its strict scoring system.[106] The test provider has minimal influence over the score, because the patients fill in the test themselves.

2.5 Outcome of elective craniotomy patients

2.5.1 Short-term morbidity and mortality

Short-term morbidity and mortality are usually defined in neurosurgery as the immediate postoperative period of up to 30 days. Morbidity associated with elective cranial neurosurgery comprises two distinct categories: systemic or infectious complications and surgery-related (neurological) complications. The former are similar to those from other types of major surgery: cardiovascular complications such as PMI or heart failure, infections such as pneumonia or sepsis, and thromboembolic complications such as pulmonary embolism (PE) or deep venous thromboembolism (DVT). The surgery-related complications reflect the delicate operative field and often have a major impact on postoperative functional status: new or worsened hemiparesis, postoperative hemorrhage or stroke, cranial nerve lesions, meningitis, and CSF leakage. Furthermore, elective craniotomy patients are prone to minor complications, much like any surgical patient. These include minor infections such as urinary tract infection (UTI) and postoperative wound infections (WIs). In modern elective neurosurgery, even cosmetic outcome is considered important, and techniques ensuring minimal visual scars or other permanent defects are desirable.[107]

Mortality is a crude outcome measure, but still often serves in evaluating and measuring the quality of health care, including neurosurgery. Many factors appear to impact mortality rates in neurosurgical patients; this has led to harsh criticism against use of mortality rates or mortality indices for outcome comparisons between

treatment centers.[108] In modern neurosurgery, expected mortality rates in western neurosurgical units are low.[109] A trend toward increasing mortality in neurosurgical patients has appeared in hospitals with a lower percentage of elective neurosurgical cases, in Level 1 trauma centers, and in hospitals not certified as stroke centers. This trend, however, fails to reach statistical significance.[108] During the past two decades, age has ceased to be a contraindication for cranial neurosurgery, and mortality rates even in the elderly have dropped.[110]

Prospective outcome reports for unselected elective craniotomy patients are lacking. A recent large retrospective cohort of over 16,000 patients undergoing elective or emergent neurosurgical procedures came out of the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) database. It showed the rate of postoperative morbidity to be 15.8% and mortality 1.6% at 30 days.[109] Furthermore, the rate of postoperative morbidity (20.1%) and mortality (2.1%) was considerably higher if a resident was the operating surgeon together with an attending, whereas patients with an attending as the only operating surgeon had significantly lower morbidity (11.7%) and mortality (1.6%) rates at 30 days ($p<0.001$ for both morbidity and mortality).[109] It should be noted, however, that both elective and emergency patients were included in the analyses; both cranial and spinal neurosurgical procedures were retrieved from the database, and thus these numbers cannot reliably reflect the short-term morbidity and mortality rates for elective cranial neurosurgery.

In a large, retrospective analysis of administrative data for 34,256 surgical patients treated during 2010 in 12 hospitals in the United States, patients undergoing intracranial procedures had the highest complication rates at discharge: 17.1%.[111] Furthermore, a retrospective analysis of over 10,000 cranial neurosurgical patients in 400 hospitals identified by means of Current Procedural Terminology (CPT) codes from the ACS NSQIP database reported a complication rate of 23.6%.[112] The American Association of Neurological Surgeons' (AANS) National Neurosurgery Quality and Outcomes Database launched in March, 2012, relies on prospectively collected outcomes data, and a module for patients undergoing intracranial surgery is expected to be implemented in the near future.[113]

Comparison of reported short-term morbidity figures in cranial neurosurgical patients is hampered by diverse definitions of morbidity; this is evident in the wide range of morbidity and mortality rates across studies. Outcome reports for unselected series of elec-

tive craniotomy patients are lacking, numbering only two reports with very narrow definitions for morbidity. According to these two studies, morbidity rates were 5.5% to 7.7%,[114, 115] and mortality rates 7.3% to 8.0%.[114] In patients with malignant tumors, reported short-term morbidity rates range from 15.0% to 35.0% and short-term mortality rates from 1.5% to 3.0%.[81, 83, 90-93] For patients with benign tumors, short-term morbidity rates range from 42.7% to 60.0%,[82, 94] whereas short-term mortality rates range from 0.0% to 23.0%.[75, 80, 82, 94] Studies on patients with unspecified intracranial tumors report short-term morbidity rates from 3.0% to 41.7%,[86-89] and short-term mortality rates from 1.2% to 3.6%.[86, 88, 89] In intracranial vascular surgery patients, short-term morbidity rates range from 8.4% to 56.0%[97, 101] and short-term mortality of 1.6%.[101]

2.5.2 Long-term morbidity and mortality

In contrast to short-term morbidity, the underlying diagnosis or disease has a greater impact on long-term morbidity and mortality. Long-term (≥6 months) outcome for patients with malignant tumors, for example, is for the large part determined by progression, location, and histological type of malignancy.

No long-term data on unselected series of elective craniotomy patients have appeared. A retrospective study on 4907 patients with metastatic brain tumors reported a long-term morbidity rate of 8.9% and long-term mortality rate of 4.0%.[99] For patients with benign tumors, the reported long-term morbidity rates range from 9.4% to 21.0%,[75, 84, 94, 100] and long-term mortality rates from 3.2% to 16.7%.[75, 78-80, 82, 84, 100] In patients undergoing craniotomy for vascular indications, long-term morbidity rates range from 14.9% to 16.5%,[85, 96] and long-term mortality rates from 0.0% to 5.0%.[85, 96, 97]

2.5.3 The mRS as a proxy for surgical outcome

Neurosurgical units worldwide have adopted the mRS as a proxy for surgical outcome, even though the original purpose of the mRS was to measure functional outcome in patients recovering from spontaneous stroke.[70] The mRS serves as a measure of outcome not only in clinical work but also for research purposes, both in cranial tumor surgery[116-118] and in cerebrovascular surgery,[119-129] including the most influential studies in the field.[16-18, 20] Evidence for the validation of the mRS as a surrogate outcome measure in neurosurgery is, however, lacking.

2.5.4 Quality of life

Quality of life (QOL) following elective cranial neurosurgery is mainly determined by the patients' postoperative neurological deficits. Postoperative systemic and infectious complications, however, can also exert a deleterious effect on functional recovery. A prolonged need for pain medication or corticosteroids or both, along with depression, has reportedly lowered postoperative QOL in patients with skull-base chordomas.[130] In patients with malignant intracranial tumors, adjuvant therapies such as whole-brain radiotherapy or local radiation therapy may have a profound impact on quality of life.[131, 132] In a recent prospective study on 180 Italian patients scheduled for neurosurgical operations, the European Health Interview Survey -Quality of Life (EUROHIS-QOL) 8-item index was useful as a quality-of-life measurement technique.[133]

2.5.5 Patient-reported outcomes (PROs) and patient-reported outcome measures (PROMs)

PROs are tools for implementing a patient-centered focus on outcome reporting in health care. The US Food and Drug Administration defines a PRO as "a report that comes directly from the patient about the status of a patient's health condition without amendment or interpretation of the patient's response by a clinician or anyone else."[134] Current focus on quality of care and public outcome reporting has made PROs a hot topic across the field of health care in recent years. In a very recent study on intracranial tumor patients, PROs were more sensitive than hospital records in identifying postoperative new or worsened neurological deficits.[135]

PROMs are either generic or disease-specific validated tools or instruments for reporting PROs.[136] It is important to distinguish PROMs from patient-reported experience measures (PREMs) such as structured patient-satisfaction questionnaires which focus on the patient's experience and the humaneness of care rather than on physical symptoms and health-related quality of life.[136] PROMs are often in the form of self-completed questionnaires,[137] so the response rate plays an important role in credibility. Modern web-based surveys provide easy access and real-time availability of data,[138] but conventional paper questionnaires may achieve better response rates.[139]

PROMs aim at improving patient safety and can guide clinicians and hospitals in decision-making. PROMs also benefit patients by enabling comparisons between hospitals, thus facilitating treatment choices. The implementation of PROMs in patient-centered outcomes research (PCOR) and clinical practice has been led by primary care

and psychiatry, with the clearest benefits emerging in the diagnosis of depression.[136] Other specialties, including surgery, have gradually adopted PROMs as tools for research and quality-improvement initiatives. Both disease-specific and generic PROMs are routine in outcome-reporting for hip and knee surgery.[140] Recently, the applicability of two PROMs, the 12-item World Health Organization Disability Assessment Schedule (WHODAS-12) and the 8-item EUROHIS-QOL, in an unselected cohort of 180 Italian neurosurgical patients has been reported in two articles by Schiavolin and coworkers.[133, 141] They were able to confirm the factor structure and validity of these PROMs, and their conclusions could support the use of these PROMs in neurosurgery departments.

Routine implementation of PROMs has proven successful in Sweden with its national quality registers since 1975.[142, 143] Since 2009, a mandatory audit of all providers of hip- and knee-replacement, varicose-vein surgery, and groin-hernia repair in England has accumulated comprehensive PROMs data.[144] Such data can serve to improve care in three ways: assisting clinicians to provide better and more patient-centered care, assessing and comparing provider quality, and providing data for evaluating practices and policies.[136]

2.5.6 Patient satisfaction

In the era of patient-centered health care, institutions and care-providers are undertaking surveys of patient satisfaction at an increasing rate. In the United States, the Centers for Medicare and Medicaid Services announced a new reimbursement method in 2011 based on patient satisfaction.[23] Patient satisfaction scores are publicly displayed online to enable open comparison between treatment centers in New South Wales, Australia.[145] Due to its being feasibly collectable, patient satisfaction has emerged as a popular proxy for quality of care. It is, however, important to distinguish between patient experience and treatment outcomes and not to confuse methods of measuring each dimension of health care quality.[146] High-quality care and good patient satisfaction can be achieved simultaneously,[147, 148] but their direct correlation has been questioned.[149] In surgical patients, poor satisfaction is commonly believed to represent poor-quality care. Overall satisfaction has not, however, proved a reliable measure of quality of care.[150-152] In spine surgery patients, patient satisfaction is a poor surrogate either for the quality or the effectiveness of care.[153] Overall satisfaction ratings in large register-based studies in surgical patient are high,[147, 149] but specific figures for cranial neurosurgery are lacking.

3. AIMS OF THE PRESENT STUDY

The objective of the present study was to evaluate preoperative risk-assessment methods, short-term outcomes, and patient satisfaction in elective cranial neurosurgery.

The specific aims of this study were to determine the

1. current state of knowledge as to the use of preoperative risk-assessment scores for elective craniotomy patients (I)

2. short-term complication types and rates after elective cranial neurosurgery (II, III, IV)

3. applicability of variables and scores currently in use for preoperative risk prediction in elective craniotomy cranial neurosurgery (II)

4. reliability of patient-reported outcomes and mRS in outcome reporting after elective craniotomy (III, V)

5. overall satisfaction of elective craniotomy patients and correlations between patient experience and short-term outcome (IV).

4. PATIENTS AND METHODS

4.1 Methods of the systematic review (I)

Study I was a qualitative systematic review of the current evidence in the literature on the use of preoperative risk-assessment scores in elective cranial neurosurgery. MEDLINE, Embase, and Pubmed databases served for identifying English-language articles published between January 1, 1980 and November 14, 2013. The initial search yielded 2229 articles, of which 128 reported original data for at least 30 patients and were selected for full-text review. Articles were excluded if they reported survival as the only outcome, they included only emergency operations, used scales with intraoperative variables, or reported less than 24-hour follow-up periods. Due to possible publication bias, in cases in which only one eligible study reported on a specific preoperative risk-assessment score, that study was excluded (9 studies). Furthermore, no reviews and commentaries were included in Study I. The final number of studies in Study I was 25. Study I followed the PRISMA guidelines for systematic reviews. Due to the extreme heterogeneity of the studies, quantitative analyses (meta-analyses) were impossible.

4.2 Patients (II-V)

Helsinki University Hospital is a public non-profit organization with 22,000 employees providing tertiary health-care services for 1.6 million people in the Helsinki area. With over 1.6 million outpatient visits and 90,000 surgeries each year, it is the second largest hospital organization in the western world. Its Department of Neurosurgery, famous for its cerebrovascular surgery, is among the largest neurosurgical centers in western countries with 3,600 surgeries annually, 18 to 19 specialist neurosurgeons, 5 operating rooms, and 250 employees.

A total of 644 patients underwent craniotomy surgery in the Department of Neurosurgery in Helsinki University hospital during the study enrollment period between 7 December, 2011 and 31 December, 2012. Informed consent was obtained from 419 patients, while 226 were either excluded (93), not reached preoperatively (85), or withheld consent to participate (47). One patient withdrew her

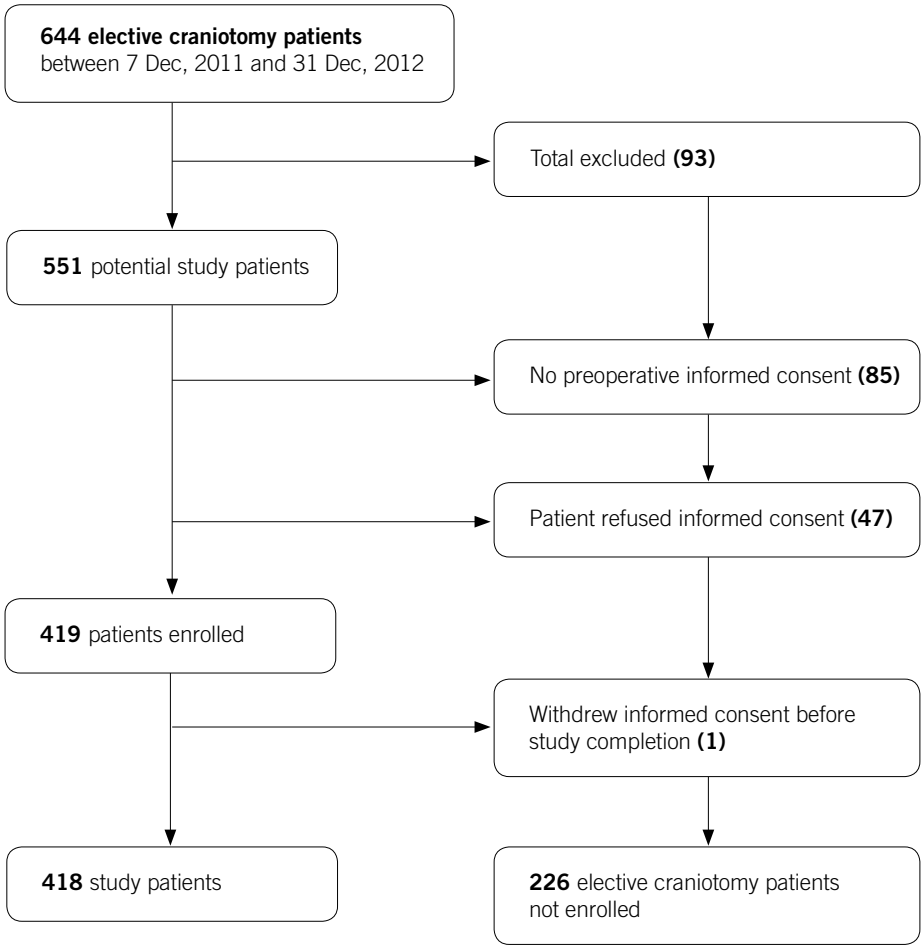
informed consent before the study ended. The exclusion criteria are summarized in Table 6. The final number of participants was 418, 75.9% of those eligible. The study flow-chart is presented in Figure 1. An elective operation was defined as a scheduled operation for which the decision to operate was made at least 7 days prior to surgery. For Patient characteristics in all patients and in indication subgroups see Table 7. To our knowledge, this is the first study on an unselected, prospective cohort of elective craniotomy patients.

Table 6. Study exclusion criteria

	Number of patients
Age under 18 years	33
Inability to communicate due to severe illness or advanced cognitive dysfunction	11
Non-fluency in Finnish or Swedish	34
Craniotomy for epilepsy (implantations of electrode grids for electro-corticographic recordings and/or subsequent resections of epileptogenic zones)	10*
Previous enrollment in study	11

* 6 patients also under 18 years old

Figure 1. Study flow-chart.



Adapted from "Preoperative identification of neurosurgery patients with a high risk of in-hospital complications: a prospective cohort of 418 consecutive elective craniotomy patients" by Reponen et al., *Journal of Neurosurgery*: September 2015 – Volume 123 – Issue 3 – p 594-604 (Study II). Printed with permission from the American Association of Neurological Surgeons©.

Table 7. Patient characteristics and perioperative variables.

Variables	Vascular lesion n=138	Benign tumor n=135	Malignant tumor n=121	Other n=24	All N=418
Age (years)	55.8 (25-75)	57.5 (19-87)	56.8 (18-85)	51.5 (19-73)	56.4 (18-87)
mean (range)	58.5	59.0	57.0	52.5	58.0
median					
Sex, n (%)					260 (62.2)
female	94 (68.1)	90 (66.7)	60 (49.6)	16 (66.7)	158 (37.8)
male	44 (31.9)	45 (33.3)	61 (50.4)	8 (33.3)	
BMI					
mean (range)	26.8 (18.8-47.4)*	26.5 (16.4-44.8)	26.1 (18.5-40.9)†	27.5 (20.1-43.8)	26.5 (16.4-47.4)‡
median	26.0*	25.5	25.8†	26.2	25.7‡
Medical history, n (%)					44 (10.5)‡
Heart condition	14 (10.1)	18 (13.4)††	9 (7.4)	3 (12.5)	54 (12.9)‡
Arrhythmia	21 (15.2)	19 (14.2)††	12 (9.9)	2 (8.3)	38 (9.1)‡
Dyspnea	14 (10.1)	12 (8.9)††	11 (9.1)	1 (4.2)	51 (12.2) ‡
Chronic lung illness	23 (16.7)	11 (8.1)††	15 (12.4)	2 (8.3)	7 (1.7)‡
Atherosclerosis, carotid stenosis, claudication	5 (3.6)	0 (0.0)††	2 (1.7)	0 (0.0)	
DVT, PE, thrombogenic condition					20 (4.8)‡
Stroke, ICH	9 (6.5)	3 (2.2)††	7 (5.8)	1 (4.2)	61 (14.6)‡
Cancer	39 (28.3)	9 (6.7)††	11 (9.1)	2 (8.3)	125 (29.9)‡
Diabetes mellitus	17 (12.3)	10 (7.4)††	97 (80.2)	1 (4.2)	47 (11.2)‡
Epilepsy	18 (13.0)	9 (6.7)††	16 (13.3)†	4 (17.4)‡‡	84 (20.1)‡
Other significant illness	18 (13.0)	19 (14.1)††	43 (35.5)	4 (16.7)	255 (61.2)‡
	89 (64.5)	88 (65.7)††	60 (49.6)	18 (75.0)	
Preoperative anticoagulants, n (%)					
Warfarin	4 (2.9)	2 (1.5)	1 (0.8)	1 (4.2)	8 (1.9)
LMWH	3 (2.2)	1 (0.7)	5 (4.1)	1 (4.2)	10 (2.4)
Warfarin with LMWH bridge	1 (0.7)	3 (2.2)	3 (2.5)	0 (0.0)	7 (1.7)
Dabigatran	0 (0.0)	1 (0.7)	0 (0.0)	0 (0.0)	1 (0.2)
Preoperative antithrombotic agents, n (%)					
Acetosalicylic acid	20 (14.5)	19 (14.1)	8 (6.6)	2 (8.3)	49 (11.7)
Clopidogrel	6 (4.3)	1 (0.2)	1 (0.8)	1 (4.2)	9 (2.2)
Acetosalicylic acid and clopidogrel	2 (1.4)	0 (0.0)	0 (0.0)	0 (0.0)	2 (0.5)
Acetosalicylic acid and dipyridamole	6 (4.3)	0 (0.0)	1 (0.8)	4 (16.7)	8 (1.9)
In-hospital mortality, n (%)	0 (0.0)	3 (2.2)	1 (0.8)	0 (0.0)	4 (1.0)
30-day mortality n (%)	0 (0.0)	4 (3.0)	6 (5.0)	0 (0.0)	10 (2.4)
ICU LOS (days)					
mean (range)	1.4 (1-13)	1.4 (0-13)	1.1 (1-5)	1.0 (1)	1.3 (0-13)
median	1.0	1.0	1.0	1.0	1.0

→

Hospital LOS (days)					
mean (range)	5.8 (2-17)	5.7 (1-34)	5.4 (1-23)	4.9 (1-14)	5.6 (1-34)
median	5.0	4.0	5.0	4.0	5.0
Location n (%)					314 (75.1)
supratentorial	119 (86.2)	80 (59.3)	102 (84.3)	13 (54.2)	104 (24.9)
infratentorial	19 (13.8)	55 (40.7)	19 (15.7)	11 (45.8)	
Surgeon n (%)	138 (100.0)				
Neurosurgeon	0 (0.0)	134 (99.3)	111 (91.7)	24 (100.0)	407 (97.4)
Resident		1 (0.7)	10 (8.3)	0 (0.0)	11 (2.6)
GA‡ n (%)					292 (70.0)
Anesthesiologist	109 (79.0)	98 (73.1)	70 (57.9)	15 (62.5)	125 (30.0)
Resident	29 (21.0)	36 (26.9)	51 (42.1)	9 (37.5)	
Anesthetic n (%)					
volatile	37 (26.8)	10 (7.4)	9 (7.4)	18 (75.0)	60 (14.4)
propofol	89 (64.5)	116 (85.9)	102 (84.3)	4 (16.7)	325 (77.8)
both	12 (8.7)	9 (6.7)	10 (8.3)	1 (4.2)	32 (7.7)
N20	50 (36.2)	28 (20.7)	12 (9.9))	6 (25.0)	96 (23.0)
Positioning n (%)					
supine	113 (81.9)	73 (54.1)	79 (65.3)	8 (33.3)	273 (65.3)
prone	0 (0.0)	6 (4.4)	8 (6.6)	0 (0.0)	14 (3.3)
sitting	8 (5.8)	8 (5.9)	8 (6.6)	2 (8.3)	26 (6.2)
park bench	16 (11.6)	45(33.3)	21 (17.4)	12 (50.0)	94 (22.5)
other	1 (0.7)	3 (2.2)	5 (4.1)	2 (8.3)	11 (2.6)
Extubation** n (%)					
in OR	85 (61.6)	63 (47.4)	69 (57.0)	21 (91.3)	238 (57.3)
in ICU < 6 hours	48 (34.8)	58 (43.6)	47 (38.8)	2 (8.7)	155 (37.3)
in ICU ≥ 6 hours	5 (3.6)	12 (9.0)	5 (4.1)	0 (0.0)	22 (5.3)
Blood loss in OR‡ (ml)					
mean (range)	88.9 (0-1600)	201.8 (0-1500)	171.5 (0-1300)	71.3 (0-400)	148.4 (0-1600)
median	50.0	100.0	100.0	40.0	100.0
Duration of operation (min)					
mean (range)	130 (59-452)	182 (65-767)	179 (66-550)	113 (42-203)	160 (42-767)
median	111	146	153	110	128
Duration of GA (min)					
mean (range)	164 (87-485)	218 (88-794)	217 (97-611)	152 (52-284)	196 (52-794)
median	147	175	193	150	162.5

* n=137, † n=120, ‡ n=417, **n=415, †† n=134, ‡‡n=23

BMI, Body Mass Index; DVT, deep vein thrombosis; GA, general anesthesia; ICH, intracranial hemorrhage; ICU, intensive care unit; LMWH, low molecular weight heparin; LOS, length of stay; N_2O; nitrous oxide; OR, operating room; PE, pulmonary embolism.

4.3 Methods (II-V)

4.3.1 Study design

The study design was prospective, observational, and aimed at collection of an unselected cohort of patients undergoing elective craniotomy in the Department of Neurosurgery, Helsinki University Hospital, Helsinki, Finland. Participation in the study did not affect the preoperative, intraoperative or postoperative care, all of which adhered to the department's standard treatment protocols.

4.3.2 Study protocol and data collection

All patients scheduled for an elective craniotomy either visited the preoperative outpatient clinic (243 patients, 58.1%) for preoperative surgical and anesthesiological evaluation or were admitted in the neurosurgical ward (175 patients, 41.9%) the day before surgery for preoperative evaluations. Patients received verbal and written information about the study after which they gave their informed consent. Patients agreeing to participate completed the preoperative forms at this stage. Preoperative laboratory testing (Table 8) and clinical evaluation, including measurement of systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR), adhered to the department's standard practice. Additional tests were performed if considered appropriate by the evaluating anesthesiologist or surgeon.

Table 8. Routine preoperative laboratory tests for elective craniotomy patients

Blood count	blood hemoglobin (Hb), g/l
	blood hematocrit (Hcr), %
	blood erythrocyte count, E12/l
	erythrocyte mean cell volume (MCV), fl
	erythrocyte mean cell Hb (MCH), pg/cell
	erythrocyte mean cell Hb concentration (MCHC), g/l
	blood leucocyte count, E9/l
	blood platelet count, E9/l
Electrolytes	plasma potassium (K), mmol/l
	plasma sodium (Na), mmol/l
Renal function	plasma creatinine (Crea), µmol/l
Infection	plasma C-reactive protein (CRP), mg/l
Glucose	plasma glucose (Gluc) not fasting, mmol/l
Coagulation	plasma prothrombin time (PT), %

The patients received detailed information on continuing or discontinuing their normal medications prior to the surgery. In particular, patients received routine instructions for the discontinuation of anticoagulant or antithrombotic medications unless there was a compelling reason to proceed with the surgery even if discontinuation of such medication was impossible. Warfarin is routinely discontinued 5 days prior to elective craniotomy at our institution. If the indication for warfarin is other than sole atrial fibrillation, or the atrial fibrillation is complicated by other problems such as cardiac failure, a low molecular weight heparin (LMWH) is substituted during warfarin discontinuation.

At our institution, for patients on continuous acetosalicylic acid medication, and whose circulatory status allows, acetosalicylic acid is discontinued for at least 5 days prior to the elective craniotomy. If the patient's circulatory status does not allow for discontinuation of acetosalicylic acid, indications for elective craniotomy are reviewed, and timing carefully reconsidered; surgery may be postponed until acetosalicylic acid can be safely discontinued. The assessing anesthesiologist gives instructions on discontinuation of other types of anticoagulant or antithrombotic medication on an individual case-by-case basis.

Study personnel collecting all data were separate from the clinical staff. Preoperative data were available from a preoperative questionnaire (Appendix 1) and from a preoperative TYM questionnaire. One of the study anesthesiologists or a study nurse completed a preoperative study form. Perioperative data were collected manually from the operating room and laboratory databases as well as from hospital patient records. Postoperative data were collected through a patient-completed questionnaire (Appendix 2), and a second TYM questionnaire identical to the one preoperatively. One of the study anesthesiologists completed a postoperative study form at discharge. One study anesthesiologist conducted a structured telephone interview to record postoperative outcome data and patient satisfaction at 30 days after surgery. The information obtained was supplemented when necessary with patient information derived from hospital patient records and clinical information systems. All data were then manually transferred to International Business Machines (IBM®) Software Package for Statistics and Simulation (SPSS®) 21.0 statistical software for statistical analysis.

4.3.3 Preoperative variables and scores

Preoperatively collected information included patient characteristics (sex, age, height, and weight), Body Mass Index (BMI), and preoperative living arrangements (home, assisted residency, nursing home, health-care center, or hospital). Patients reported the health conditions listed in Table 9 (yes/no; diagnosis and when diagnosed)

Table 9. Preoperative health conditions.

Condition	Patients (%) N=417
Heart condition	44 (10.6)
Arrhythmia	54 (12.9)
Dyspnea	38 (9.1)
Chronic lung illness	51(12.2)
Atherosclerosis, carotid artery stenosis, claudication	7 (1.7)
Deep vein thrombosis, pulmonary embolism, thrombogenic condition	20 (4.8)
Stroke, intracranial hemorrhage	61 (14.6)
Cancer	125 (30.0)
Diabetes mellitus*	47 (11.3)
Epilepsy	84 (20.1)

*N=415

Questions on health-related habits were adapted from the Health 2000 survey of the National Public Health Institution in Finland.[154] Selected questions covered smoking (number of cigarettes per day, smoking years, when ceased) and alcohol consumption (none, moderate, excessive) within the past 7 days. Moderate alcohol consumption was defined as 1 to 16 doses for women and 1 to 24 doses for men. Alcohol consumption exceeding 16 doses (women) and 24 doses (men) was categorized as excessive. Patients reported their preoperative average frequency of physical exercise (duration at least 20 minutes, sufficiently intensive to cause shortness of breath) on a 5-tier scale: none (unable due to illness or physical condition), less often than once a week, once a week, 2 to 3 times a week, or 4 times a week or more. Stair-climbing served as a measure of cardiorespiratory fitness.[155] A flight of stairs was defined as a vertical climb between two floors (at least 4 meters), and patients reported whether they could climb two flights of stairs without resting, and if not, why. Fur-

thermore, patients categorized their preoperative subjective overall health status and physical fitness as excellent, good, average, poor or very poor. The detailed questions are in Appendix 1. Additionally, the patients completed the TYM questionnaire preoperatively.

At the time of the preoperative consultation, the neuroanesthesiologist recorded data on date of operation, place of preoperative consultation and basic patient characteristics. Other recorded variables included medications affecting blood coagulation (acetosalicylic acid, dipyridamole, warfarin, LMWHs, clopidogrel, novel oral anticoagulants including dabigatran and rivaroxaban), preoperative blood pressure, heart rate, laboratory measurements (Table 8), and possible preoperative neurological symptoms.

Preoperative scores included the Charlson comorbidity score, original ASA classification score (Table 1), preoperative mRS score (Table 3), and the modified Helsinki ASA classification score in clinical use in the Department of Neurosurgery, Helsinki University Hospital, since the mid 1990's (Table 10). Other preoperatively recorded variables comprised location of the craniotomy (supratentorial or infratentorial), indication for surgery (malignant tumor, benign tumor, vascular indication, or other indication), and experience of the operating surgeon and of the attending anesthesiologist (specialist/resident).

Table 10. Helsinki ASA classification

Helsinki ASA score	Description
1	Previously healthy patient, age <65 years
2	Previously healthy patient, age ≥65 years Patient with mild systemic disease
3	Patient with severe systemic disease Previously healthy patient <65 years, with a small unruptured intracranial aneurysm or a small brain tumor with no symptoms/mild symptoms
4	Patient with unbalanced systemic disease Previously healthy patient with a clearly symptomatic intracranial aneurysm or brain tumor
5	Moribund patient not expected to survive without emergency surgery

4.3.4 Perioperative variables

The data collected also included perioperative variables. Duration of anesthesia and surgery (in minutes) came from the operating room database along with information concerning patient positioning during surgery (supine, prone, lateral park bench, sitting, or other position), intraoperative blood loss, time of extubation [in the operating room, in the intensive care unit (ICU) postoperatively <6 hours, or ≥6 hours] and choice of anesthetic (propofol, volatile anesthetic, or both, and whether also nitrous oxide was used).

4.3.5 Postoperative in-hospital variables and scores

The recorded postoperative variables and scores included date of discharge from the hospital (length of stay), and place discharged to (home, assisted living, nursing home, health-care center, or hospital). Patients were invited to report any postoperative neurological symptoms or deficits and were specifically asked about new or worsened hemiparesis, subjective visual disturbances (SVD), speaking difficulties (dysphasia, dysarthria), dysphagia, local WI or asymptomatic meningitis, other infections, stroke or cerebral ischemia, pneumonia, thromboembolic complications (PE, DVT) and heart attack (Appendix 2).

Furthermore, the patients reported whether their subjective functional status had changed during hospitalization (better, unchanged, or worse). The postoperative TYM score and the mRS score assigned by a study anesthesiologist were recorded at hospital discharge. Length of ICU stay in days as well as blood hemoglobin (Hb) concentration on the first postoperative morning were recorded, together with possible reoperations and prolonged problems of ventilation or dysphagia necessitating tracheostomy. An anesthesiologist also recorded possible complications and neurological symptoms at hospital discharge. The rate of in-hospital mortality was available from the Population Register Center of Finland and from hospital databases, the latter also providing additional information on postoperative complications and neurological sequelae.

Complication phenotypes served for association analyses in Study III. Ranking the complications was based on univariable analyses with an mRS-score difference ≥3 at between preoperative and hospital discharge scores. This cutoff value represents an increase which results in a dependent functional status for a preoperatively

asymptomatic (mRS score 0) patient. Complications reaching significance in univariable analyses were then entered into multivariable logistic regression analysis. After multivariable analysis, the most significant complications were first ranked in order. Second came all major, followed by all minor complications which failed to reach statistical significance; these were ranked in order by frequency. For each patient, his/her highest-ranking complication phenotype was the one assigned.

4.3.6 30-day outcome variables and scores

Those patients surviving the 30-day follow up were contacted by telephone, and a study anesthesiologist conducted a structured interview. The questions addressed possible remaining neurological symptoms attributable to the surgery, severity of the possible symptoms (none, mild, or severe) and postoperative living arrangements (dependence on the aid of relatives or nursing staff). The mRS was re-assessed by means of a validated telephone mRS questionnaire.[31] In addition, the patients reported their perceived overall health status (excellent, good, average, poor, very poor), and their overall satisfaction (excellent, good, satisfactory, poor, very poor) with the treatment they received during hospitalization. For statistical analyses, severity of symptoms was categorized as insignificant (none or mild) or significant (severe), overall health as good (average, good, or excellent) or poor (poor or very poor), and patient satisfaction as high (good or excellent) and low (satisfactory, poor, or very poor).

After the 30-day follow-up, a study anesthesiologist manually retrieved data on reoperations involving the head for the time period between hospital discharge and the end of the 30-day follow-up. The Population Register Center of Finland provided 30-day mortality data for the study cohort.

4.3.7 Study outcome measures

We recorded both in-hospital and 30-day mortality rates. Mortality, however, is a crude outcome measure in the context of elective cranial neurosurgery, with statistically significant associations expected only in very large cohorts. Thus, composites of short-term adverse events (complications/morbidities) were our choice as primary outcome measures, inclusive or noninclusive of in-hospital mortality depending on the situation. Additionally, resource use [ICU and in-hospital length of stay (LOS)] served as an outcome measure (Study II).

4.3.7.1 New CNS deficits (II)

In Study II, one outcome comprised new permanent or transient central nervous system (CNS) deficits defined as new or worsened hemiparesis, or stroke (clinical and/or radiological).

4.3.7.2 Systemic and infectious complications (II)

Systemic and infectious complications in Study II comprised the following conditions recorded during hospitalization or at hospital discharge: DVT, PE, acute myocardial infarction (AMI), pneumonia, and WI or asymptomatic meningitis.

4.3.7.3 Major morbidity (III, IV, V)

For Studies III, IV, and V, short-term postoperative complication categories included major and minor complications. The composite outcome measure "major morbidity" used in these three studies comprised new or worsened hemiparesis, silent stroke, DVT, PE, AMI, pneumonia, in-hospital mortality (unless otherwise specified), and unplanned re-craniotomy (CRT) or endovascular intervention (EI) within the 30-day follow-up (Table 11).

4.3.7.4 Overall morbidity (III, IV, V)

Overall morbidity was defined in studies III and IV as major and/or minor morbidity. The short-term postoperative adverse events categorized as minor morbidity were: asymptomatic meningitis/WI, minor infections such as urinary tract infection or conjunctivitis, SVD, new or worsened facial nerve palsy, dysphasia or dysarthria, dysphagia, and unplanned minor cranial reoperations such as ventriculostomy or wound revision in the OR (Table 11).

Table 11. Study outcome measures.

Time of recording			Any time during hospitalization	At hospital discharge, max 30 days	30 postoperative days
Data collection methods			• Patient-reported questionnaire • Anesthesiologist-completed study form • Systematic manual retrieval from hospital patient records by study anesthesiologist		• Anesthesiologist-completed study form • Systematic manual retrieval from hospital patient records/ OR-management database by study anesthesiologist
Overall morbidity	Major morbidity			• In-hospital mortality*	• 30-day mortality* • Unplanned re-CRT or EI
		New CNS deficits	• Silent stroke	• New or worsened hemiparesis	
		SI complications	• AMI • Pneumonia • PE • DVT		
	Minor morbidity		• Minor infections • SVD • New or worsened facial nerve palsy • Dysphasia or dysarthria • Dysphagia	• WI or asymptomatic meningitis	• Unplanned minor cranial reoperations (in OR) – ventriculostomy – wound revision

AMI, acute myocardial infarction; CNS, central nervous system; CRT, craniotomy; DVT, deep venous thromboembolism; EI, endovascular intervention; OR, operating room; PE, pulmonary embolism; SI, systemic and infectious; SVD, subjective visual disturbances; WI, wound infection.

*Unless otherwise specified

Adapted from "Patient satisfaction and short-term outcome in elective cranial neurosurgery" by Reponen et al., Neurosurgery: November 2015 – Volume 77 – Issue 5 – p 769-776 (Study IV). Printed with permission from Wolters Kluwer Health Lippincott Williams & Wilkins©

4.3.8 Statistical methods

The IBM® SPSS® 21.0 statistical software for Microsoft (MS®) Windows and Macintosh Operating System (Mac OS®) X served for statistical analyses. Nominal data is presented as numbers (percentages). Odds ratios (ORs) and 95% confidence intervals (CIs) are reported where appropriate. The statistical tests and statistics included the Pearson Chi Square test or Fisher's Exact test for categorical variables (II, III, IV, V), the Mann-Whitney U-test or Kruskall-Wallis test for continuous or ordinal variables (II, III, IV, V), and multivariable logistic regression analyses (II, III, V). Furthermore, sensitivity (III, V) specificity (III, V), positive predictive value (PPV) (III), and negative predictive value (NPV) (III) were calculated for outcome predictors and measures. In all analyses, significance was at $p<0.05$.

4.3.8.1 Pearson Chi Square test

The Pearson Chi Square test is applicable for unpaired categorical data from large samples. It is calculated by cross tabulation of the categorical variables, which should be mutually exclusive. Two conditions must be met: first, a maximum of 20% of the expected values can be less than five, and second, none of the expected values can be less than one. The test evaluates the statistical significance of the differences of the observed frequency ratios in the contingency table. In other words, it tests how likely it is that any distribution observed is due to chance. The null hypothesis is no statistical dependence between variables. The Chi Square test is meant to test the probability of independence of a distribution of data, but will not clarify the quality of the relationship between variables. Furthermore, for contingency tables larger than 2 x 2, post hoc analyses are essential to determining those groups between which the difference is statistically significant.

4.3.8.2 Fisher's Exact test

Fisher's exact test is usually applied to unpaired categorical data in small samples if conditions for the Pearson Chi-Square test are unmet. It is valid, however, for all sample sizes. Fisher's Exact test examines the significance of any association between the two groups. The p-value is computed as if the margins of the table are fixed. The null hypothesis is independence.

4.3.8.3 Odds ratio

Odds ratio (OR) is a measure of the effect size describing the strength of association or nonindependence between two binary variables. OR is calculated by dividing the ratio of positive observations to negative observations in group A by the ratio of positive observations to negative observations in group B. If OR equals one, no difference exists between the two groups. If OR is greater than one, the ratio of positive-to-negative observations in group A is greater than in group B. If OR is less than one, the ratio of positive-to-negative observations in group A is smaller than in group B. A 95% CI is usually reported along with OR to help determine the statistical significance. If the number "1" is included in the CI, the difference is not statistically significant.

4.3.8.4 Mann-Whitney U-test

The Mann-Whitney U-test, also known as the Wilcoxon 2-sample test or Wilcoxon rank-sum test, examines two independent samples (groups). It is the nonparametric equivalent for Student's t-test. This test is applicable when a numeric variable is not normally distributed or the variable is ordinal. This test compares differences in location of the distribution of two independent samples, the null hypothesis being no difference. Rather than using the actual observed values in the calculations, the Mann-Whitney U-test is based on assigned numeric ranks for all observations and involves calculating rank sums in order to gain the U-statistic and p-value.

4.3.8.5 Kruskall-Wallis test

The Kruskall-Wallis test is the nonparametric equivalent of one-way analysis of variance (ANOVA), and tests whether samples originate from the same distribution. This test does not assume normal distribution. The Kruskall-Wallis test, an extension of the Mann-Whitney U-test, serves to compare two or more independent samples. If the null hypothesis is rejected, at least one group statistically differs from at least one other group. The Kruskall-Wallis test does not, however, identify where this occurs or for how many pairs of groups, but post-hoc tests (pairwise Mann-Whitney U-tests, with their p-values corrected with, for example, Bonferroni correction) are necessary. Like the Mann-Whitney U-test, the Kruskall-Wallis test is based on assigned ranks and rank sums.

4.3.8.6 Linear and logistic regression analyses

Linear regression analysis examines the linear association between independent and dependent variables, both of which are numeric. The model can include one or multiple independent variables. The method assumes independence of the observations, a linear association between the independent and dependent variables, a normal distribution of the dependent variable with every combination of independent variables, and homoscedasticity (homogeneity of variance).

Logistic regression analysis is applicable to situations in which the dependent variable is categorical. The model can include one or multiple categorical or numerical covariates or both. If the dependent variable is binary, the method is called binary logistic regression.

A rule of thumb dictates that one independent variable or covariate for each ten observations can be added to the model. Selecting the independent variables and covariates requires solid theoretical knowledge of the field. Selection is usually based on statistical significance. The independent variables or covariates selected should be tested by collinearity diagnostics because strong intercorrelations would lead to multicollinearity.

4.3.8.7 Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV)

Sensitivity and specificity measure the performance of a binary test such as a diagnostic test with either a positive or a negative result. Sensitivity measures the proportion of true positives correctly identified as such. In other words, sensitivity is the percentage of sick people who are correctly identified by a positive result in a diagnostic test (true-positive rate). Specificity describes the proportion of true negatives correctly identified as such. Thus, specificity is the percentage of healthy individuals who are correctly identified by a negative result in a diagnostic test (true-negative rate) (Figure 2).

PPV is the proportion of positive results in a diagnostic test that are true positives. In other words, PPV is the probability that patients with a positive test result in fact have the disease. NPV is the proportion of negative results in a diagnostic test that are true negatives. NPV is the probability that patients with a negative test result are in fact healthy. Like its sensitivity and specificity, PPV and NPV describe the performance of a diagnostic test. PPV and NPV depend on the prevalence of the condition (Figure 2).

Figure 2. Calculating sensitivity, specificity, PPV, and NPV.

	sick	healthy	
test positive	a	b	a+b
test negative	c	d	c+d
	a+c	b+d	N=a+b+c+d

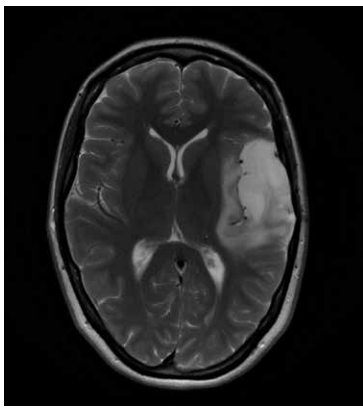
Sensitivity= a/(a+c) PPV= a/(a+b)
Specificity= d/(b+d) NPV= d/(c+d)

4.3.8.8 Receiver operating characteristics (ROC) curve and area under the curve (AUC)

The ROC curve is a graph of the positive likelihood ratios in which the Y axis represents the proportion of true-positive results (sensitivity) and the X axis represents the proportion of false-positive results (1 minus specificity). A ROC curve serves for presenting the characteristics of a diagnostic test. The area under the ROC curve (AUC) represents the accuracy of the diagnostic test in detecting the disease and ranges from 0.5 (worthless test) to 1.0 (perfect test). An AUC of 0.5 indicates that the test results are no better than chance, and the test with the largest AUC is considered the most accurate.

4.3.9 Ethical aspects

The study protocol was reviewed and approved by the ethics committee and the institutional board of the Hospital District of Helsinki and Uusimaa. The study was observational in design, and all preoperative, perioperative, and postoperative evaluations and treatments adhered to the standard clinical practice of the Department of Neurosurgery. Each patient signed an informed consent prior to enrollment and all were informed of their right to withdraw from the study at any point. Completing the questionnaires was not considered a burden for the patients, because the number of questions was limited, and completing the questionnaires took only a few minutes. Severely ill patients or patients with advanced cognitive dysfunction, for whom participating would have caused too much strain or who were unable to understand the study protocol, were excluded. Nonparticipation or withdrawal had no effect on the patients' clinical treatment.



MR image showing a low-grade glioma in the temporal lobe and adjacent insular cortex.

5. RESULTS

5.1 Results of the systematic review (I)

Study I included 25 studies, each reporting the use of at least one preoperative risk-assessment score.

5.1.1 ASA Physical Status Classification score

Evidence for use of the ASA classification in elective cranial neurosurgery is scarce. In Study I, we reported a total of 10 studies that assess the role of the ASA classification in preoperative risk prediction.[75, 78-80, 82-85, 114, 115] Only two of these studies clearly stated whether the surgeries were elective, emergency or a collection of both. Only one study was prospective. Eight studies, including the only prospective study, reported a positive association between the ASA classification and outcome. The main shortcomings of the existing studies were poorly defined outcome, relatively small size (<300 patients) in 8, retrospective design in 9, and failure to report short-term (<30-day) morbidity and mortality in 5 studies.

In two retrospective studies, the primary outcome was surgery-related. The conclusions of the two studies were contradictory: in one, on patients with unruptured intracranial aneurysms (157 craniotomies), only calcification of the aneurysm correlated with poor outcome (Glasgow Outcome Scale <4) at 6 months,[85] whereas in elderly meningioma patients, a preoperative ASA score of 3 or 4 predicted a Karnofsky Performance Score (KPS) of 70 or less at the 4-month follow-up.[78]

In two studies with nonsurgical outcomes, a preoperative ASA score ≥2 predicted surgical site infections,[115] and higher preoperative ASA scores were associated with an increased incidence of postoperative meningitis.[114]

An association between preoperative ASA score 3 or more and postoperative morbidity emerged in two retrospective studies on patients with meningiomas and malignant tumors.[82, 83] Mortality was the primary outcome in four retrospective studies on elderly patients with intracranial meningiomas;[75, 79, 80, 84] three of these studies reported a significant association between high ASA scores and mortality,[75, 79, 84] whereas one study confirmed no such association.[80]

In conclusion, the role of the ASA classification in predicting outcome after elective cranial neurosurgery is somewhat ambiguous (Table 12). Evidence suggests that it may be useful for predicting infectious complications and, possibly, postoperative functional status.[78, 114, 115]

5.1.2 KPS score

Our systematic review (Study I) provided 16 studies on the applicability of KPS to preoperative outcome prediction in cranial neurosurgery.[75, 78-81, 83, 84, 86-94] Of these studies, three were prospective.[81, 91, 92] Only one study reported whether the surgeries were elective, emergency, or both.[81] Altogether 14 studies concluded that a positive association existed between KPS and postoperative outcome.[75, 78-81, 83, 84, 86, 87, 89, 91-94]

Six studies assessed KPS in predicting a surgery-related outcome.[78, 81, 88, 91, 93, 94] The results of two prospective studies[81, 91] and three retrospective studies[78, 93, 94] supported the use of KPS. KPS predicted neurological outcome in 21-day follow-up in a prospective cohort of over 400 patients with malignant gliomas.[91] No significant change in preoperative versus postoperative KPS at 6 months was detectable in a prospective study of patients with high-grade gliomas, indicating a positive prognostic association.[81] A retrospective study of patients with insular gliomas concluded that a high preoperative KPS was associated with a favorable outcome (KPS >80) in a 3-month follow up. Preoperative KPS 70 or less was predictive of a poor postoperative outcome (KPS 70 or less) in elderly patients with intracranial meningioma.[78] In patients with meningiomas, KPS was associated with early (1 week) but not late (3 months) neurological deficits.[94] One study reported no significant association between preoperative KPS and postoperative neurological status or operative complications in intra-axial brain tumor patients.[88]

Three retrospective studies reported associations between KPS and nonsurgical outcomes.[86-88] Low preoperative KPS associated with postoperative systemic complications such as pneumonia, acute heart failure, acute renal failure, and sepsis in elderly patients with intracranial tumors during a 4-week follow-up.[86] A retrospective study with a large cohort (over 4000 patients) with intracranial tumors reported a significant association of preoperative KPS 70 or less with the development of DVT or PE within 30 days after craniotomy.[87] No significant association between preoperative KPS and systemic complications was identifiable in patients with intra-axial brain tumors.[88]

Five studies reported overall morbidity as their outcome.[83, 88-90, 92] In patients with supratentorial tumors, KPS 50 or less correlated with a complicated outcome (neurological, medical, or operative complications).[89] KPS associated with postoperative complications, including hematomas, local infections, fistulas, thromboembolic complications, sepsis, and cardiac failure within a 30-day follow-up in patients with malignant intracranial tumors.[83] No association between the preoperative KPS and postoperative morbidity or 30-day mortality was identifiable in patients with gliomas/metastases and intra-axial brain tumors.[88, 90] KPS was unassociated with prolonged hospital stay, life-threatening situation, reintervention, or readmission.[90] In patients with gliomas or metastases, preoperative KPS correlated with 30-day mortality but not with morbidity.[92] A preoperatively high KPS score associated with postoperative mortality in elderly patients with meningiomas.[75, 78-80, 84]

In conclusion, KPS has substantial evidence as a risk-assessment tool for patients with intracranial tumors regardless of the nature of the tumor both for short-term[80, 83, 86, 89, 91-94] and long-term[75, 78, 80, 81, 84, 93, 94] postoperative outcomes (Table 12). Evidence supports the applicability of preoperative KPS in predicting surgery-related outcomes with a positive correlation reported in four of five studies. Furthermore, five of seven studies reported a positive correlation between low preoperative KPS and postoperative mortality.

5.1.3 mRS score

Our systematic review (Study I) found two studies using mRS for preoperative prediction of postoperative outcome in cranial neurosurgery.[96, 97] The results of the two studies were conflicting: Low mRS score was an independent predictor of surgical outcome at 1-year follow-up in patients with brainstem cavernous malformations,[97] but in patients with unruptured posterior circulation aneurysms, preoperative mRS score was a significant predictor of neither surgical morbidity nor mortality.[96] As shown in Table 12, evidence as to the applicability of mRS as a preoperative risk score in elective craniotomy patients is very limited.

5.1.4 Charlson comorbidity score

In Study I, we identified three large register-based retrospective studies on the applicability of the Charlson Comorbidity Score in preoperative risk assessment of craniotomy patients.[99-101] Two studies

included both emergency and elective patients, but for the third study this information was unavailable. The Charlson comorbidity score was associated with in-hospital mortality in patients with unruptured intracranial aneurysms.[101] In elderly patients with metastatic brain tumors, each 1-point increase in Charlson comorbidity score raised the odds of inpatient death by 12% and odds of stroke or pulmonary complications and also length of hospitalization.[99] Furthermore, the Charlson comorbidity score was associated with higher odds of inpatient death and major postoperative complications in elderly patients with intracranial meningioma.[100]

Even though all three studies suggested a positive correlation between the Charlson comorbidity score and postoperative outcome (Table 12), their results should be interpreted cautiously since two of the three came from the same authors at Johns Hopkins, in Baltimore, Maryland, so the external validity of the results may be limited.

5.1.5 SKALE score

Our systematic review (Study I) found only two retrospective studies utilizing the SKALE score.[75, 84] Each, with limited patient numbers and outcome defined as mortality at 12 months, reached the opposite conclusion. The SKALE score added no value when compared to the ASA score in predicting the postoperative outcome in meningioma patients.[84] In elderly meningioma patients, however, a SKALE score of 8 or higher was associated with a significantly reduced postoperative mortality.[75] Existing studies, thus, suggest that SKALE may be useful in predicting long-term postoperative mortality (Table 12), but studies linking preoperative SKALE score and short-term outcome are lacking.

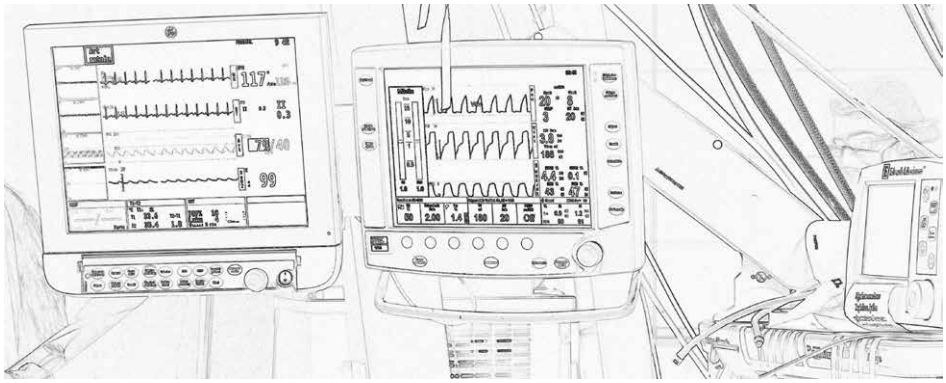


Table 12. Summary of applicability of proposed scores in elective cranial neurosurgery. Number of studies in parentheses.

	Surgery-related		Nonsurgical		Morbidity		Mortality	
	+	-	+	-	+	-	+	-
Malignant tumor	KPS (3)				ASA (1) KPS (1) Charlson (1)	KPS (2)	KPS (1) Charlson (1)	KPS (1)
Benign tumor	ASA (1) KPS (2)				ASA (1) Charlson (1)		ASA (3) KPS (4) Charlson (1) SKALE (2)	ASA (1)
Tumors (not specified)		KPS (1)	KPS (2)	KPS (1)	KPS (1)	KPS (1)		KPS (1)
Vascular	mRS (1)	ASA (1) mRS (1)					Charlson (1)	mRS (1)
Mixed			ASA (2)					

+, study results support use; -, study results do not support use; ASA, American Society of Anesthesiologists Physical Status Score; Charlson, Charlson comorbidity score; KPS, Karnofsky Performance Score; mRS, modified Rankin Scale; SKALE, Sex, Karnofsky, ASA, Location, Edema -score.

5.2 Short-term postoperative complications (II, III, IV) and complication phenotypes (III)

In-hospital complication data were available for all 418 study patients. A total of 194 (46.4%) patients suffered from overall morbidity, whereas the rate of major morbidity (including in-hospital mortality) was 18.2% (76 patients) (IV). The most common major complication was new or worsened hemiparesis (41 patients, 9.8%). The rate of unplanned re-craniotomy or endovascular intervention was 4.1% (17 patients). Pneumonia was diagnosed in 14 (3.3%) patients. Silent stroke was detectable in the radiological imaging studies of 6 (1.4%) patients. Other major complications were rare; AMI in 4 patients (1.0%), PE in 3 (0.7%), and DVT in 2 (0.5%).

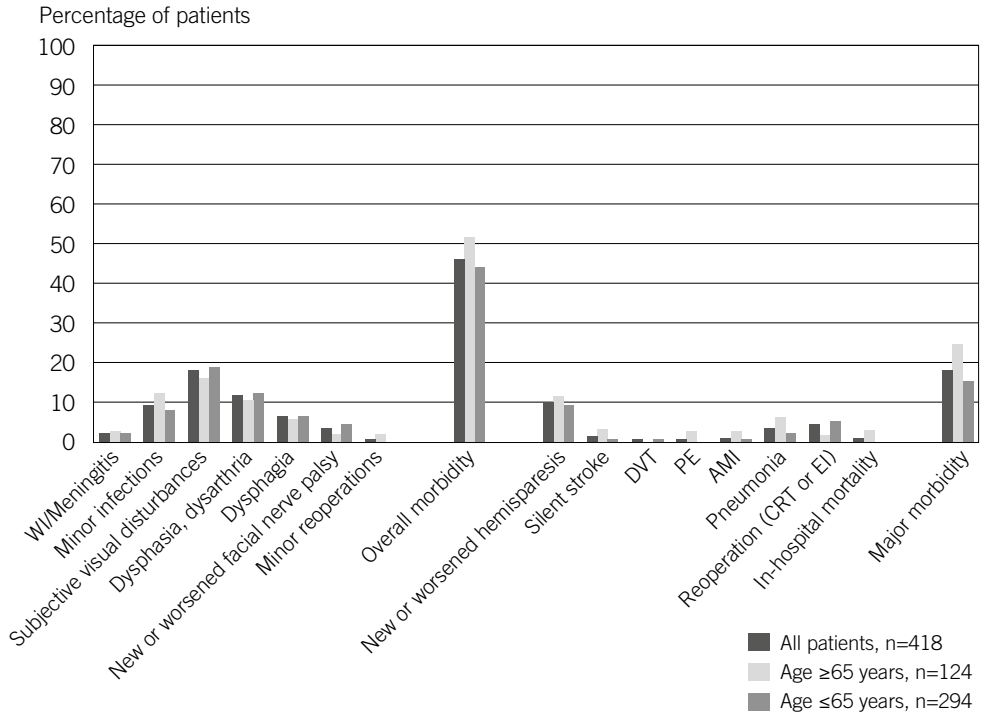
In the 121 patients with malignant tumors as an indication for the craniotomy, the rates of new or worsened hemiparesis (17 patients, 14.0%), re-craniotomy or endovascular intervention (7, 5.8%), DVT (2, 1.7%), and PE (2 patients, 1.7%) were higher than in the whole study cohort. The 135 patients undergoing craniotomy for benign tumors had higher rates of silent strokes (3 patients, 2.2%), AMI (3, 2.2%), and re-craniotomy or endovascular intervention (8, 5.9%) than did the whole cohort. The 138 cerebrovascular surgery patients (n=138) less frequently had new hemiparesis (10 patients, 7.2%),

silent stroke (1 patient, 0.7%), and recraniotomy or endovascular intervention (1, 0.7%) but more frequently pneumonia (6, 4.3%) than did the whole study cohort.

Altogether 159 patients (38.0%) suffered from minor complications, 118 of them without any major complication. The minor complication most frequently reported was SVD in 76 patients (18.2%). The rate of dysphasia or dysarthria was 11.7% (49) and minor infections were recorded in 39 (9.3%). Dysphagia was recorded in 26 patients (6.2%). Rare conditions were new or worsened facial nerve palsy (14 patients, 3.3%), WI/meningitis (9 patients, 2.2%), and unplanned minor cranial reoperations in the OR (3 patients, 0.7%).

The complication profile in patients aged ≥65 years differed from that of younger patients. The elderly were more susceptible to infectious complications, major new CNS defects, PE, AMI, and suffered more in-hospital mortality (Figure 3). The rate of major complications in the subgroup of elderly patients was 25.0% and of overall complications, 51.6%.

Figure 3. Complication rates in age subgroups.



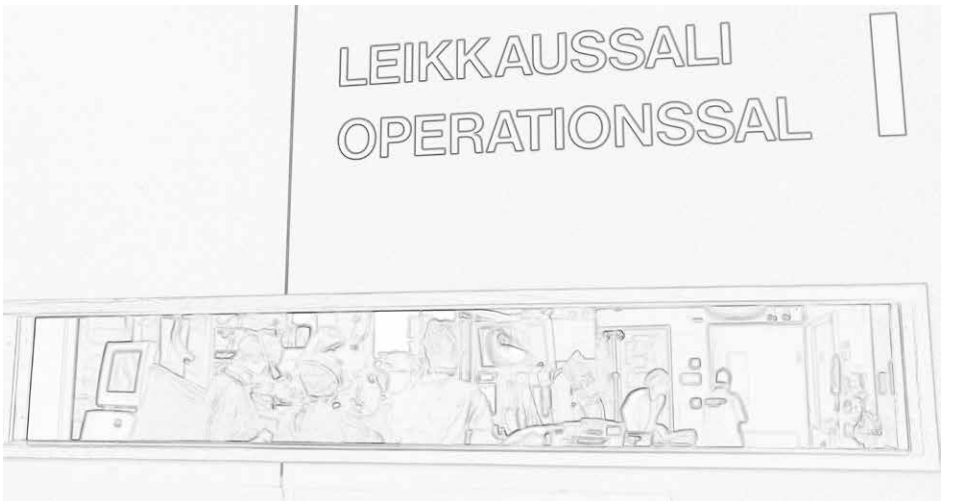
AMI, acute myocardial infarction; CRT, craniotomy; DVT, deep venous thromboembolism; EI, endovascular intervention; PE, pulmonary embolism; WI, wound infection.

After multivariable analyses for complication phenotypes, only three individual complications retained their significance (III). New or worsened hemiparesis (p<0.001), silent stroke (p<0.001), and pneumonia (0=0.005) were associated with an mRS-score difference >2 from preoperative to hospital discharge score. For complication phenotypes, see Table 13.

Table 13. Complication phenotypes in 194 patients with reported postoperative complications.

Complication phenotypes ranked in order	Patients, n=194
Hemiparesis	41
Silent stroke	6
Pneumonia	8
re-CRT or EI	14
AMI	2
PE	2
DVT	2
SVD	64
Speech impairment	25
Minor infection	19
Dysphagia	7
Facial nerve palsy	2
Meningitis/WI	2
Minor cranial reoperation	0

AMI, acute myocardial infarction; CRT, craniotomy; DVT, deep venous thromboembolism; EI, endovascular intervention; PE, pulmonary embolism; SVD, subjective visual disturbances; WI, wound infection



5.3 Outcome measures

5.3.1 New CNS deficits (II)

New CNS deficits were identified in 47 (11.2%) patients (II). Of the surgical indications, patients with malignant tumors had the highest rate of new CNS deficits, 15.7% (Table 14).

5.3.2 Systemic and infectious complications (II)

Systemic and infectious complications occurred in 28 (6.7%) patients (II). One-eighth (12.1%) of elderly patients (≥65 years) and one-tenth (10.4%) of patients with preoperative C-reactive protein (CRP) >3 mg/l suffered from systemic and infectious complications (II). For rates of systemic and infectious complications in various patient subgroups, see Table 14.

5.3.3 Major morbidity (III-V)

The rate of major morbidity in the whole study cohort was 18.2% (76 patients) (III, IV). Elderly patients had a higher major morbidity rate than did the whole cohort, also by patient subgroup (Table 14). Especially in patients undergoing intracranial vascular surgery, the rate of major morbidity almost doubled in patients aged ≥65.

5.3.4 Overall and minor morbidity (III-V)

Altogether 194 patients suffered from at least one of the recorded complications, making the overall morbidity rate 46.4%. Minor complications occurred in 159 (38.0%) patients, of whom, 118 (74.2%) had no major morbidity. Patients aged ≥65 with intracranial vascular surgery had the highest rates of overall (69.0%) and minor (65.5%) morbidity. Elderly patients with benign tumors, when compared with all benign tumor patients, had a lower rate of overall morbidity (47.7% versus 51.1%) (Table 14) and minor morbidity (29.5% versus 43.0%).

5.3.5 In-hospital and 30-day mortality (II-V)

Altogether 4 study patients died during the in-hospital period and an additional 6 within the 30-day follow-up. Thus, the in-hospital mortality rate was 1.0%, and 30-day mortality rate 2.4% (Table 14). All deceased patients were 64-year-olds or older. The characteristics of the deceased patients and their specific postoperative complications are in Table 15.

Table 14. Frequencies of new CNS deficits, systemic and infectious complications, major morbidity, overall morbidity, in-hospital mortality and 30-day mortality in various patient subgroups.

	New CNS deficits	SI complications	Major morbidity	Overall morbidity	In-hospital mortality	30-day mortality
Patient subgroup (N)	Patients (%)	Patients (%)	Patients (%)	Patients (%)	Patients (%)	Patients (%)
All (418)	47 (11.2)	28 (6.7)	76 (18.2)	194 (46.4)	4 (1.0)	10 (2.4)
Age ≥65 years (124)	18 (14.5)	15 (12.1)	31 (25.0)	64 (51.6)	4 (3.2)	9 (7.3)
Vascular (138)	11 (8.0)	10 (7.2)	15(10.9)	62 (44.9)	0 (0.0)	0 (0.0)
Age ≥65 years (29)	3 (10.3)	4 (13.8)	6 (20.7)	20 (69.0)	0 (0.0)	0 (0.0)
Benign tumor (135)	17 (12.6)	8 (5.9)	29 (21.5)	69 (51.1)	3 (2.2)	4 (3.0)
Age ≥65 years (44)	7 (15.9)	4 (9.1)	11 (25.0)	21 (47.7)	3 (6.8)	4 (9.1)
Malignant tumor (121)	19 (15.7)	10 (8.3)	31 (25.6)	55 (45.5)	1 (0.8)	6 (5.0)
Age ≥65 years (45)	8 (17.8)	7 (15.6)	13 (28.9)	22 (48.9)	1 (2.2)	5 (11.1)

Table 15. Characteristics of the 10 deceased patients.

Patient number	Age (years)	Sex	Indication	Comorbidities	Postoperative complications
1	75	Female	Benign tumor	Atrial fibrillation Cerebrovascular incident Diabetes mellitus	AMI
2	67	Female	Benign tumor	Problems with memory	Stroke Tracheostomy
3	85	Female	Benign tumor	3rd degree AV-block with pacemaker Toxic struma Rhabdomyolysis 1 month before surgery	Sudden death*
4	66	Male	Malignant tumor (metastasis)	Endocarditis 1 month before surgery Stroke 2 months before surgery Cancer with brain metastasis, primary focus unknown Hypertension Hypercholesterolemia	Stroke AMI Pneumonia
5	64	Male	Malignant tumor	WPW syndrome Previous DVT and PE Epilepsy Hypothyroidism	DVT
6	84	Male	Malignant tumor	Lymphoma Crohn's disease	Pneumonia
7	77	Male	Malignant tumor	Previous AMI Exposure to asbestos	Hemiparesis
8	85	Male	Malignant tumor	Atrial fibrillation Psoriatic arthritis	Pneumonia
9	65	Male	Malignant tumor	Previous AMI Asthma, COPD Previous pneumonia Previous PE APC resistance (coagulation abnormality)	Urinary tract infection
10	85	Female	Benign tumor	CAD Hypertension Glaucoma	Dysphagia

Patients 1-4 died before hospital discharge. Patients 5-10 died after being discharged from Töölö hospital, within 30 days of the primary operation.

AMI, acute myocardial infarction; AV, atrioventricular; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; DVT, deep venous thromboembolism; PE, pulmonary embolism; WPW, Wolff-Parkinson-White.

*Asystole and resuscitation on 3rd postoperative day, massive PE in autopsy.

5.3.6 Length of stay (LOS)

5.3.6.1 ICU LOS (II)

The mean ICU LOS was 1.3 days [standard deviation (SD) 1.4] and median 1.0 (range 0-13) (II). The ICU stays in patient subgroups by surgical outcome measures are presented in Table 16. In patients aged ≥65 years, the mean ICU LOS was 1.4 days (SD 1.2) and median 1.0 (range 1-11).

5.3.6.2 Hospital LOS (II)

The mean hospital LOS was 5.6 days (SD 3.5 days) and median 5.0 days (range 1-34 days) (II). The hospital stays in patient subgroups by surgical outcome measures are in Table 16. In elderly patients, the mean hospital LOS was 6.1 days (SD 3.3) and median 5.0 (range 1-16).

Table 16. ICU and hospital LOS in patient subgroups by surgical outcome measures.

	Patient subgroups		
	No complications	Major morbidity	Overall morbidity
	n=224	n=76	n=194
ICU LOS in days mean (SD) median (range)	 1.0 (0.2) 1.0 (0-2)	 2.3 (2.9) 1.0 (0-13)	 1.6 (2.0) 1.0 (0-13)
Hospital LOS in days mean (SD) median (range)	 4.6 (2.3) 4.0 (1-23)	 8.1 (5.7) 6.0 (2-34)	 6.7 (4.2) 6.0 (1-34)

ICU, intensive care unit; LOS, length of stay, SD, standard deviation

5.4 Preoperative risk-assessment methods

5.4.1 Preoperative risk-assessment scores

5.4.1.1 ASA Physical Status score (II)

Preoperative ASA scores were available for 417 (99.8%) patients. For their distribution, see Figure 3. Of patients aged ≥65 years, 17 (13.7%) had preoperative ASA score 4. In Study II, preoperative ASA score groups did not differ with regard to systemic and infectious complications (p=0.213), new CNS deficits (p=0.408), ICU LOS (p=0.095), or hospital LOS (p=0.389). The associations of high preoperative ASA score with study outcome measures are in Table 17. Of individual complications, only AMI (p=0.031, OR and CI not calculable), dysphagia

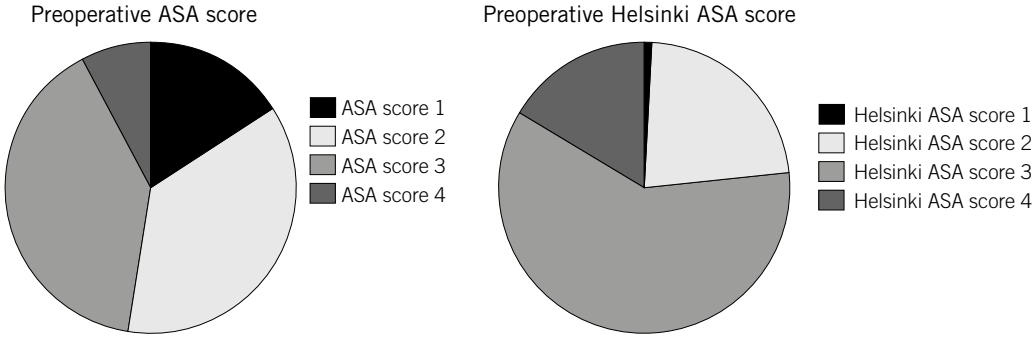
(p=0.010, OR 4.2, CI 1.6-11.4), and minor cranial reoperations in the OR (p=0.016, OR 25.6, CI 2.3-290.5) were statistically associated with preoperative ASA score >3.

5.4.1.2 Helsinki ASA score (II)

Preoperative Helsinki ASA scores were available for 417 patients. For their distribution, see Figure 4. The preoperative ASA score was 4 for 33 (26.6%) patients aged ≥65. In Study II, Helsinki ASA 2 group differed from the Helsinki ASA 3 (p=0.027) or Helsinki ASA 4 (p=0.002) groups in predicting systemic and infectious complications. The Helsinki ASA groups did not differ with regard to new CNS deficits (p=0.663) (II). The Helsinki ASA 4 group had longer ICU stays than did the Helsinki ASA 2 (p=0.015) or Helsinki ASA 3 (p=0.013) groups (II). Additionally, the Helsinki ASA 2 group had shorter hospital stays than did the Helsinki ASA 3 (p=0.022) or Helsinki ASA4 (p=0.001) groups (II). These associations remained significant after multivariable logistic regression analyses (categorical outcome variables) and multivariable linear regression analyses (continuous outcome variables) (II).

Table 17 presents the associations between high preoperative Helsinki ASA score and study outcome measures. The only individual complications associated with preoperative Helsinki ASA score >3 were pneumonia (p<0.001, OR 10.5, CI 3.4-32.4) and dysphagia (p=0.023, OR 3.0, CI 1.3-7.0).

Figure 4. Distribution of preoperative ASA scores and Helsinki ASA scores. Only elective craniotomy patients were enrolled and thus no patients with scores >4 were included in the study cohort.



ASA score	Patients (%) N=417	Helsinki ASA score	Patients (%) N=417
1	67 (16.1)	1	4 (1.0)
2	152 (36.5)	2	94 (22.5)
3	166 (39.8)	3	251 (60.2)
4	32 (7.7)	4	68 (16.3)

ASA, American Society of Anesthesiologists Physical Status Classification.

Table 17. Associations of preoperative ASA score (>3), Helsinki ASA score (>3), mRS score (>2), and Charlson comorbidity score (>2) with study outcome measures and AUC for each test. Significant associations in bold, Fisher's Exact test results italicized.

	New CNS deficits							
	p	OR	95%CI	sens (%)	spec (%)	PPV (%)	NPV (%)	AUC
ASA	0.155	1.9	0.8-5.0	12.8	93.0	18.8	89.4	0.503
Helsinki ASA	0.328	1.5	0.7-3.1	21.3	84.3	14.7	89.4	0.543
mRS	***0.043***	2.3	1.0-5.2	19.1	90.8	20.9	89.8	0.572
Charlson	0.323	1.4	0.7-2.7	31.9	74.8	13.9	89.6	0.579
	Systemic and infectious complications							
	p	OR	95%CI	sens (%)	spec (%)	PPV (%)	NPV (%)	AUC
ASA	0.256	2.1	0.7-6.6	14.3	92.8	12.5	93.8	0.609
Helsinki ASA	***0.030***	2.6	1.1-6.1	32.1	84.8	13.2	94.6	0.655
mRS	***0.017***	3.3	1.3-8.2	25.0	90.7	16.3	94.4	0.651
Charlson	**0.003**	3.1	1.4-6.8	50.0	75.8	13.0	95.5	0.642
	Major morbidity							
	p	OR	95%CI	sens (%)	spec (%)	PPV (%)	NPV (%)	AUC
ASA	0.131	1.9	0.8-4.2	11.8	93.3	28.1	82.6	0.556
Helsinki ASA	0.114	1.6	0.9-3.0	22.4	85.0	25.0	83.1	0.567
mRS	**<0.001**	3.5	1.8-6.8	22.4	92.4	39.5	84.2	0.610
Charlson	**0.001**	2.4	1.4-4.0	40.8	77.4	28.7	85.4	0.646
	Overall morbidity							
	p	OR	95%CI	sens (%)	spec (%)	PPV (%)	NPV (%)	AUC
ASA	0.059	2.0	1.0-4.3	10.3	94.6	62.5	54.8	0.559
Helsinki ASA	**0.002**	2.3	1.3-3.9	22.3	88.8	63.2	57.0	0.577
mRS	**0.004**	2.6	1.3-5.1	14.9	93.7	67.4	55.9	0.559
Charlson	**0.009**	1.8	1.2-2.8	32.0	79.3	57.4	57.1	0.576
	In-hospital mortality							
	p	OR	95%CI	sens (%)	spec (%)	PPV (%)	NPV (%)	AUC
ASA	***0.031***	12.8	1.7-93.9	50.0	92.7	6.3	99.5	0.749
Helsinki ASA	0.126	5.3	0.7-38.0	50.0	84.0	2.9	99.4	0.729
mRS	0.055	9.1	1.2-66.1	50.0	90.1	4.7	99.5	0.627
Charlson	0.055	8.8	0.9-85.2	75.0	74.5	2.8	99.7	0.799
	30-day mortality							
	p	OR	95%CI	sens (%)	spec (%)	PPV (%)	NPV (%)	AUC
ASA	***<0.001***	14.1	3.8-51.6	50.0	93.4	15.6	98.7	0.772
Helsinki ASA	***<0.001***	13.2	3.3-52.6	70.0	85.0	10.3	99.1	0.811
mRS	***<0.001***	15.0	4.0-55.6	60.0	90.9	14.0	98.9	0.769
Charlson	***<0.001***	12.2	2.6-58.6	80.0	75.4	7.4	99.4	0.841

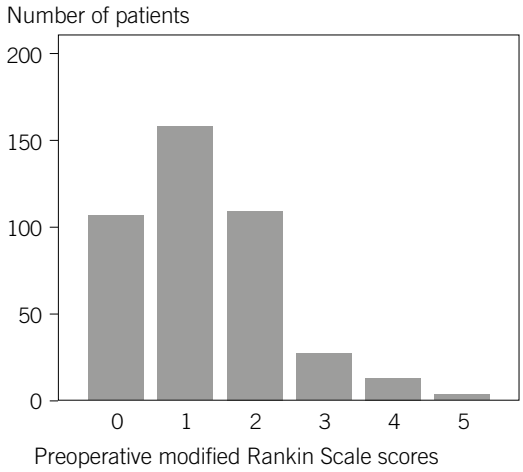
All ASA, Helsinki ASA, and mRS scores for 417 patients. Charlson comorbidity scores for 416 patients.

AMI, acute myocardial infarction; ASA, American Society of Anesthesiologists' physical status classification; Charlson, Charlson comorbidity score; CI confidence interval; CNS, central nervous system; CRT, craniotomy; DVT, deep vein thrombosis; EI, endovascular intervention; mRS, modified Rankin Scale; NPV, negative predictive value; OR, odds ratio; PE, pulmonary embolism; PPV, positive predictive value; sens, sensitivity; spec, specificity.

5.4.1.3 mRS score

A preoperative mRS score was available for 417 patients (Figure 5). The mean preoperative mRS score was 1.26 (SD 1.1) and median 1 (range 0-5). A majority of patients aged ≥65 (98 patients, 79.0%) were preoperatively functionally independent (mRS score ≤2). Table 17 shows associations between study outcome measures and high preoperative mRS score dichotomized at >2 indicating a dependent functional status. Of individual major complications, only pneumonia (p=0.001, OR 7.4, CI 2.4-22.5) was associated with high preoperative mRS score. Preoperative mRS score >2 was associated with increased hospital LOS (p=0.003) but not with increased ICU LOS (p=0.379). (Reponen et al., unpublished data)

Figure 5. Distribution of preoperative mRS scores.

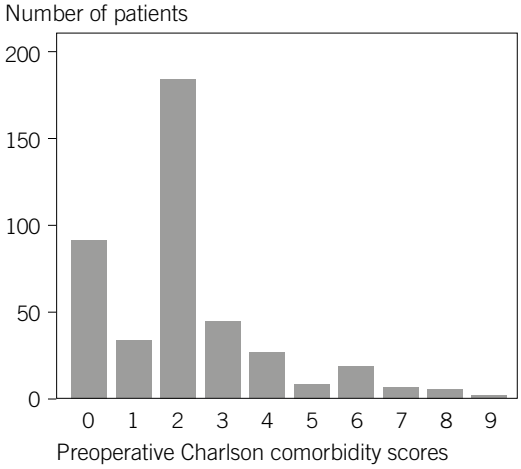


Preoperative mRS score	Patients (%) N=417
0	107 (25.7)
1	158 (37.9)
2	109 (26.1)
3	27 (6.5)
4	13 (3.1)
5	3 (0.7)

5.4.1.4 Charlson comorbidity score

Of the 416 patients with available preoperative Charlson comorbidity scores, almost three-fourths (308, 74.0%) had scores ≤2 (Figure 6). The respective mean and median Charlson comorbidity scores were 2.1 (SD 1.8) and 2.0 (range 0-9). In the subgroup of patients ≥65 years old, 70 (56.6%) had Charlson comorbidity score ≤2. Associations between study outcome measures and high preoperative Charlson comorbidity scores (dichotomized at >2) are in Table 17. Of individual major complications, only pneumonia (p=0.012, OR 4.0, CI 1.4-11.9) and PE (p=0.017, OR and CI not calculable) were associated with high preoperative Charlson comorbidity score. A preoperative Charlson comorbidity score >2 was associated with increased hospital LOS (p=0.039) but not with increased ICU LOS (p=0.350) (Reponen et al., unpublished data).

Figure 6. Distribution of preoperative Charlson comorbidity scores.



Preoperative Charlson comorbidity score	Patients (%) N=416
0	91 (21.9)
1	33 (7.9)
2	184 (44.2)
3	44 (10.6)
4	26 (6.3)
5	8 (1.9)
6	18 (4.3)
7	6 (1.4)
8	5 (1.2)
9	1 (0.2)

5.4.2 Patient characteristics, patient-reported preoperative variables and preoperative laboratory measurements (II)

Table 18 presents the preoperative clinical and laboratory measurements. Preoperative patient-reported variables are in Table 19. In univariable analyses between patient characteristics and preoperative laboratory measurements and individual major complications, significant associations were detected only between advanced age and pneumonia (p=0.004), lower Hb level and silent stroke (p=0.008), higher plasma potassium (K) level and AMI (p=0.014), higher plasma creatinine (Crea) level and PE (p=0.022), and advanced age and AMI (0.028).

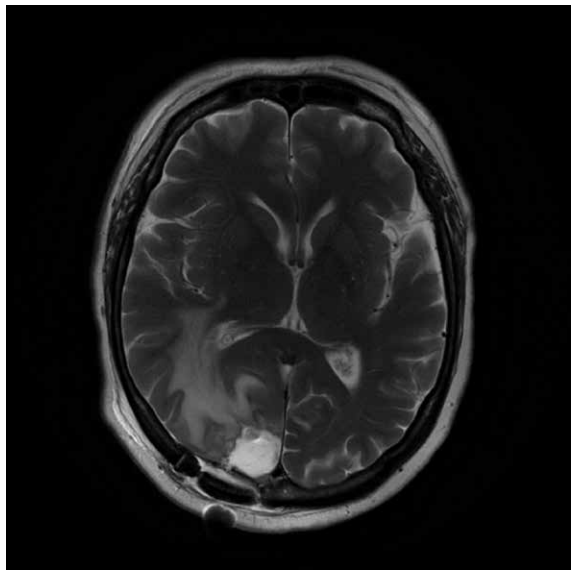
Differences in preoperatively recorded variables (age, sex, weight, height, BMI, and additional variables in Table 18) in patients with and without new CNS deficits failed to reach statistical significance (II). Of these variables, only age ≥65 (p=0.004, OR 3.0, CI 1.4-6.5, sensitivity 53.6%, specificity 72.1%, PPV 12.1%, NPV 95.6%), BMI in quartiles (p=0.024), and preoperatively elevated CRP dichotomized at >3 mg/l (p=0.046, OR 2.2, CI 1.0-5.1, sensitivity 42.3%, specificity 75.4%, PPV 10.4%, NPV 95.1%) were associated with systemic and infectious complications (II). Male sex (p=0.044, OR 1.6, CI 1.0-2.8, sensitivity 48.0%, specificity 64.4%, PPV 22.8%, NPV 85.0%) and age ≥65 (p=0.019, OR 1.8, CI 1.1-3.1, sensitivity 40.8%, specificity 72.8%, PPV 25.0%, NPV 84.7%) were the only variables associated with major morbidity. High blood glucose (p=0.032) was associated with overall morbidity. Age ≥65 was associated with both in-hospital (p=0.007, OR and CI not calculable, sensitivity 100.0%, specificity 71.0%, PPV 3.2%, NPV 100.0%) and 30-day (p<0.001, OR 22.9, CI 2.8-183.0, sensitivity 90.0%, specificity 71.8%, PPV 7.3%, NPV99.7%) mortality. Additionally, high heart rate (p=0.049), high blood glucose (p=0.006), and high preoperative CRP (0.014) were associated with in-hospital mortality. Variables associated with 30-day mortality included high heart rate (p=0.041), low thrombocyte count (p=0.036), high blood glucose (p<0.001), high preoperative CRP (p=0.021), and high plasma sodium (p=0.002).

In univariable analyses for resource use, only high blood glucose (p=0.012) and high or low potassium (p=0.025) were significant predictors of prolonged ICU LOS. Significant predictors of extended hospital LOS comprised high SBP (p=0.029), low Hb (p=0.019) (II).

Table 18. Preoperative clinical and laboratory measurements

	Patients	Mean (SD)	Median (range)
SBP (mmHg)	416	142.4 (20.5)	141 (95-224)
DBP (mmHg)	416	85.9 (11.3)	86 (46-137)
HR (beats/min)	415	70.1 (13.5)	68 (41-114)
Hb (g/l)	417	140.6 (12.2)	141 (105-180)
Platelets (E9/l)	417	245.3 (66.4)	238 (32-543)
Crea (µmol/l)	416	70.2 (16.3)	68 (5-160)
Gluc (mmol/l)	409	6.5 (2.6)	5.8 (3.9-24.8)
CRP (mg/l)	412	5.2 (7.4)	3 (3-77)
Na (mmol/l)	417	138.5 (4.0)	139 (123-158)
K (mmol/l)	417	4.0 (0.4)	4.0 (2.9-5.6)
PT (%)	410	112.2 (23.9)	108 (9-170)

SBP, systolic blood pressure; Crea; creatinine; DBP, diastolic blood pressure; Gluc, glucose; HR, heart rate; Hb, hemoglobin; CRP, C-reactive protein; Na, sodium; K, potassium; PT plasma prothrombin time.



MR image after surgery for occipital brain metastasis.

Table 19. Preoperative patient-reported variables

Variables	Vascular lesion Patients (%)	Benign tumor Patients (%)	Malignant tumor Patients (%)	Other Patients (%)	Age ≥65 years Patients (%)	All Patients (%)
Smoking						
yes	39 (30.7)	25 (21.0)	18 (17.3)	4 (18.2)	11 (10.8)	86 (23.1)
ex-smoker	54 (42.5)	32 (26.9)	35 (33.7)	8 (36.4)	36 (35.3)	129 (34.7)
no	34 (26.8)	62 (52.1)	51 (49.0)	10 (45.5)	55 (53.9)	157 (42.2)
Alcohol use within 7 days						
none	67 (55.4)	62 (52.5)	78 (75.7)	13 (59.1)	71 (71.7)	220 (60.4)
moderate	52 (43.0)	55 (46.6)	25 (24.3)	9 (40.9)	28 (28.3)	141 (38.7)
excessive	2 (1.7)	1 (0.8)	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.8)
Physical exercise habits						
never	18 (15.1)	11 (9.6)	22 (22.0)	3 (13.6)	22 (23.2)	54 (15.2)
< 1 time/week	22 (18.5)	24 (21.1)	16 (16.0)	6 (27.3)	15 (15.8)	68 (19.2)
1 time/week	19 (13.8)	21 (18.4)	21 (21.0)	3 (13.6)	13 (13.7)	64 (18.0)
2-3 times/week	33 (27.7)	35 (30.7)	25 (25.0)	6 (27.3)	26 (27.4)	99 (27.9)
≥ 4 times/week	27 (22.7)	23 (20.2)	16 (16.0)	4 (18.2)	19 (20.0)	70 (19.7)
Ability to climb 2 flights of stairs						
yes	107 (89.2)	96 (85.7)	78 (78.8)	21 (95.5)	72 (75.0)	302 (85.6)
no	13 (10.8)	16 (11.9)	21 (21.2)	1 (4.5)	24 (25.0)	51 (14.4)
Physical fitness						
excellent	5 (4.1)	9 (7.8)	5 (5.1)	2 (9.5)	2 (2.0)	21 (5.9)
good	50 (40.7)	46 (40.0)	38 (38.4)	7 (33.3)	38 (38.4)	141 (39.4)
average	53 (43.1)	46 (40.0)	37 (37.4)	6 (28.6)	37 (37.4)	142 (39.7)
poor	14 (11.4)	13 (11.3)	18 (18.2)	5 (23.8)	20 (20.2)	50 (14.0)
very poor	1 (0.8)	1 (0.9)	1 (1.0)	1 (4.8)	2 (2.0)	4 (1.1)
Overall health						
excellent	14 (10.9)	17 (13.8)	7 (6.9)	3 (14.3)	6 (5.9)	41 (10.9)
good	66 (51.2)	62 (50.4)	42 (41.2)	6 (28.6)	47 (46.1)	176 (46.9)
average	37 (28.7)	36 (29.3)	35 (34.3)	8 (38.1)	36 (35.3)	116 (30.9)
poor	12 (9.3)	7 (5.7)	17 (16.7)	3 (14.3)	12 (11.8)	39 (10.4)
very poor	0 (0.0)	1 (0.8)	1 (1.0)	1 (4.8)	1 (1.0)	3 (0.8)
Cognitive function						
normal (TYM score ≥45)	88 (69.3)	84 (70.6)	47 (50.0)	17 (81.0)	48 (48.4)	236 (65.4)
diminished (TYM score <45)	39 (30.7)	35 (29.4)	47 (50.0)	4 (19.0)	45 (51.6)	125 (34.6)

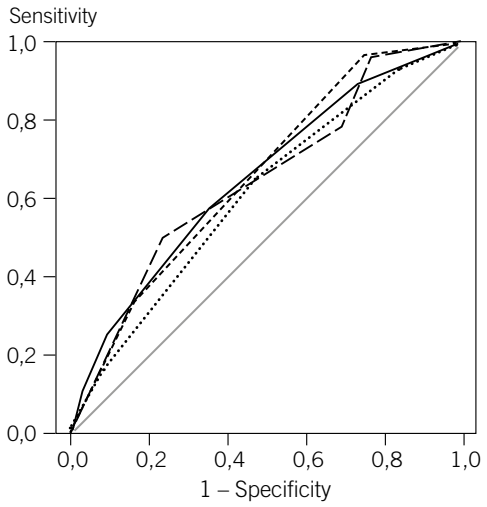
TYM, Test Your Memory. Composite preoperative risk predictors (II)

5.4.3 Composite preoperative risk predictors (II)

In Study II, all preoperative variables significantly predicting study outcome measures in univariable analyses underwent logistic regression analyses (for systemic and infectious complications) or linear regression analyses (for resource use). No significant associations were detectable between preoperative risk predictors and new CNS deficits. After multivariable analyses for systemic and infectious complications, CRP dichotomized at >3 mg/l (p=0.049), age dichotomized at ≥60 years (p=0.013), and Helsinki ASA score 4 (p=0.016) retained their statistical significance. The AUC for this model was 0.766 (p<0.001, CI 0.673-0.869) (Figure 7). Helsinki ASA score 4 was the only variable that remained a significant predictor after multivariable analyses for both ICU (p=0.004) and hospital LOS (p=0.023).

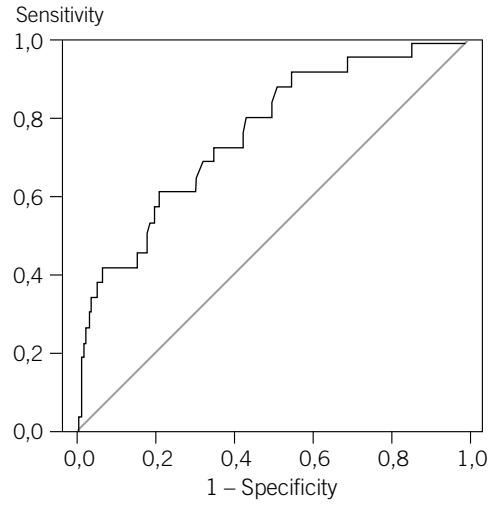
Combinations of variables retaining their significance after the multivariable analyses were evaluated to identify patients at high risk for complications and increased resource use. The combination of Helsinki ASA score 4, age ≥60 years, and preoperative CRP >3 mg/l identified almost one-fourth of patients with systemic and infectious complications (p=0.005, OR 4.8, CI 1.5-15.9, sensitivity 14.3%, specificity 96.7%, PPV 23.5%, NPV 94.0%) (II). The combination of Helsinki ASA score 4 and age ≥60 years was associated with a nearly 40% increase in ICU LOS (p=0.018) and a 20% increase in hospital LOS (p=0.004) (II).

Figure 7. ROC curves for preoperative risk scores and multivariable logistic regression model (Study II) based on the current cohort in predicting systemic and infectious complications.



Modified Rankin Scale
Charlson comorbidity score
Original ASA score
Helsinki ASA score
Reference line

Score	AUC
ASA	0.609
Helsinki ASA	0.655
mRS	0.651
Charlson	0.642



Multivariable model
Reference line

Score	AUC
Multivariable model	0.766

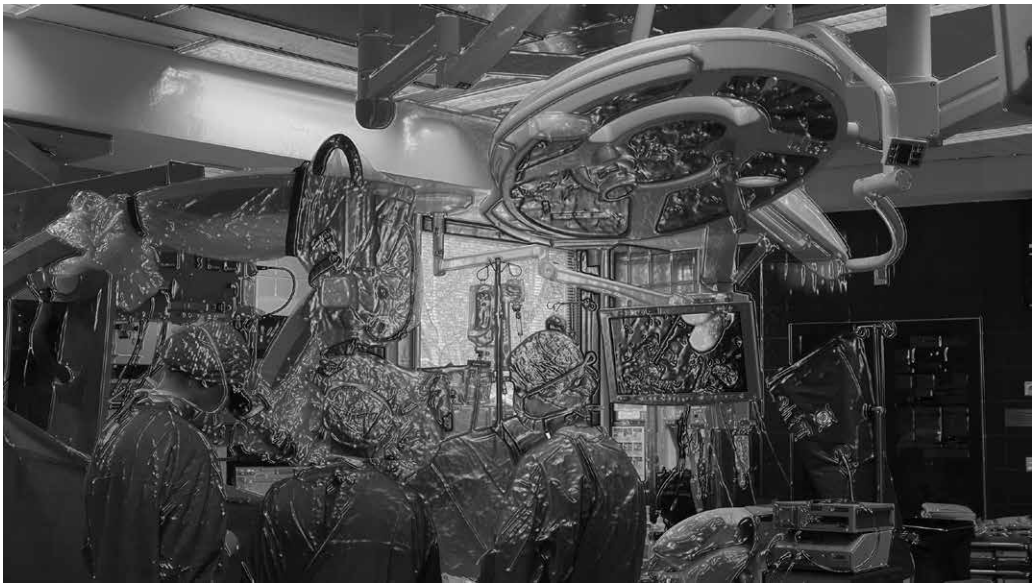
ASA, American Society of Anesthesiologists

5.5 Postoperative in-hospital assessments

5.5.1 mRS at hospital discharge (III)

A hospital discharge mRS score was available for 406 patients, including the 4 who died before discharge (mRS score 6). Respective mean and median hospital discharge mRS scores were 1.5 (SD 1.5) and 1 (range 0-6). The distribution of postoperative mRS scores is presented in Figure 8. At hospital discharge, 314 (77.3%) of all patients were functionally independent (mRS score ≤2). The corresponding numbers were 74 (61.7%) for elderly patients (≥65 years), 84 (71.2%) for patients with malignant tumors, 104 (78.8%) for those with benign tumors, and 106 (79.7%) for those undergoing cerebrovascular surgery.

Of individual major complications, mRS score at hospital discharge dichotomized at ≥3 was associated with new or worsened hemiparesis (p<0.001, OR 20.4, CI 9.0-46.4), silent stroke (p=0.003, OR 18.0, CI 2.1-156.0), AMI (p=0.003, OR and CI not calculable), and pneumonia (p<0.001, OR 51.5, CI 6.6-399.6). The rarity of individual complications resulted in very wide CIs, thus limiting the reliability of these associations. Of individual minor complications, meningitis/WI (p=0.031, OR 4.5, CI 1.2-16.9), minor infections (p=<0.001, OR 3.4, CI 1.7-6.7), and minor cranial reoperations in the OR (p=0.011, OR and CI not calculable) were associated with mRS score ≥3 at hospital

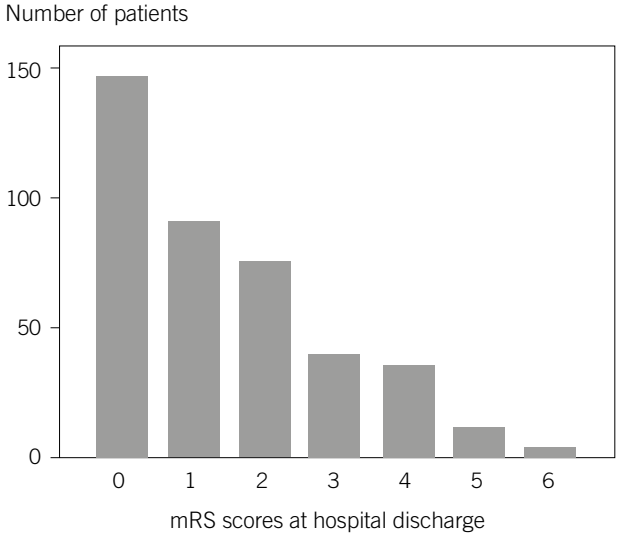


discharge. The associations of hospital discharge mRS scores with study outcome measures are presented in Table 21.

The mRS-score difference from preoperative to hospital discharge score was available for 405 patients (Figure 9). The median mRS-score difference was 0 (range -2-6). An increase in mRS score (mRS-score difference >0) was associated with the following complication phenotypes: hemiparesis (p=<0.001, OR 11.7, CI 5.0-27.2), silent stroke (p=0.008, OR 13.0, CI 1.5-112.2), pneumonia (p<0.001, OR and CI not calculable), SVD (p<0.001, OR 3.1, CI 1.7-5.6), and speech impairment (p=0.004, OR 3.3, CI 1.4-7.8).

At hospital discharge, 138 (34.1%) patients had an mRS-score difference >0 and 54 (13.3%) >1. Of 216 patients with no recorded short-term complications, their mRS score increased in 37 (17.1%). Of 75 patients with major complications, 21 (28.0%) showed no increase in mRS scores at discharge. Furthermore, of these 75 patients, 41 (54.6%) had no mRS-score difference > 1 at discharge. Only 57.6 % of all patients with mRS score ≥3 at discharge experienced major morbidity. Significant associations were detectable between study outcome measures and mRS-score difference >0 at discharge (Table 21).

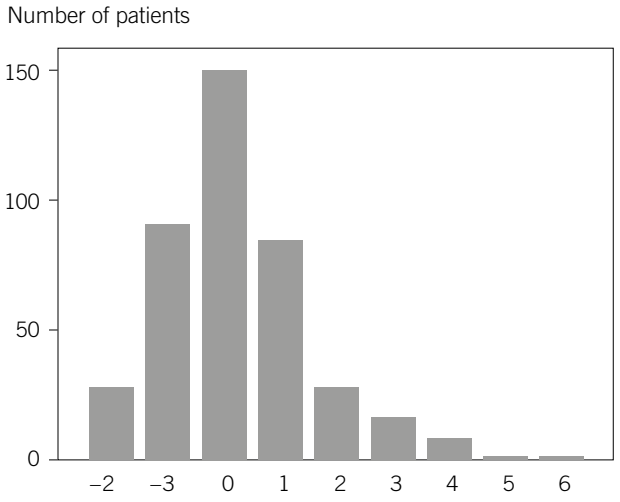
Figure 8. Distribution of mRS scores at hospital discharge



mRS score at hospital discharge	Patients (%) N=406
0	147 (36.2)
1	91 (22.4)
2	76 (18.7)
3	40 (9.9)
4	36 (8.9)
5	12 (2.9)
6	4 (1.0)

mRS, modified Rankin Scale

Figure 9. Distribution of mRS-score differences between preoperative and hospital discharge score.



mRS-score difference between preoperative and hospital discharge score	Patients (%) N=405
-2	28 (6.9)
-1	90 (22.2)
0	149 (36.8)
1	84 (20.7)
2	28 (6.9)
3	16 (4.0)
4	8 (2.0)
5	1 (0.2)
6	1 (0.2)

mRS, modified Rankin Scale

5.5.2 Postoperative patient-reported outcomes (V)

Table 20 presents the postoperative patient-reported outcomes for all study patients, indication subgroups, and the elderly. At hospital discharge, 317 (75.8%) patients reported their subjective functional status. Of 308 (73.7%) patients with available postoperative TYM scores, 238 (77.3%) had normal cognition. Subjective deterioration in functional status was associated with 30-day mRS ≥3 indicating dependent functional status ($p<0.001$, OR 3.1, CI 1.6-5.8).

Both subjective deterioration in functional status ($p<0.001$, OR 18.1, CI 5.3-61.6, sensitivity 88.9%, specificity 69.3%) and postoperatively diminished cognitive status ($p<0.001$, OR 4.3, CI 1.8-10.2, sensitivity 52.2%, specificity 79.6%) were associated with new CNS deficits but not with systemic and infectious complications.

Of 103 patients who reported postoperative subjective deterioration in functional status, major morbidity occurred in 30 (26.5%), whereas the corresponding percentage was only 5.9 when subjective functional status remained unchanged or improved. The association between major morbidity and subjective deterioration in functional status was significant in univariable analysis ($p<0.001$, OR 5.8, CI 2.8-11.8). Furthermore, this association remained significant after multivariable logistic regression analysis including all hospital dis-

charge and 30-day PROs (p=0.001, OR 4.9, CI 1.9-12.0, sensitivity 71.4%, and specificity 69.8%). In patients aged ≥65, major morbidity complicated the outcome in 10 of 18 patients with postoperative subjective deterioration in functional status (sensitivity 71.4%, specificity 74.6%). The association between postoperatively diminished cognitive status and major morbidity was also significant in univariable analysis (p=0.009, OR 2.5, CI 1.2-5.2), but not in multivariable logistic regression analysis.

Both postoperative subjective deterioration in functional status (p<0.001, OR 7.3, CI 4.3-12.3) and postoperatively diminished cognitive status (p=0.015, OR 1.9, CI 1.1-3.3) were associated with overall morbidity, but after multivariable logistic regression analysis only the association between postoperative subjective deterioration in functional status and overall morbidity remained significant (p<0.001, OR 5.7, CI 3.1-10.7, sensitivity 58.6%, specificity 83.7%).

Table 20. Postoperative and 30-day patient-reported outcomes

Variables	Vascular lesion Patients (%)	Benign tumor Patients (%)	Malignant tumor Patients (%)	Other Patients (%)	Age ≥65 years Patients (%)	All Patients (%)
Change in functional status*						
unchanged	74 (66.7)	48 (44.9)	24 (31.2)	7 (31.8)	37 (43.5)	145 (48.3)
better	4 (3.6)	16 (15.0)	21 (27.3)	10 (41.7)	20 (23.5)	51 (16.2)
worse	33 (29.7)	43 (40.2)	32 (41.6)	5 (22.7)	28 (32.9)	113 (35.6)
Cognitive function*						
normal (TYM score ≥45)	88 (63.8)	82 (79.6)	50 (68.5)	18 (81.8)	52 (62.7)	238 (77.3)
diminished (TYM score <45)	22 (15.9)	21 (20.4)	23 (31.5)	4 (18.2)	31 (37.3)	70 (22.7)
Symptom severity†						
none	43 (32.1)	35 (27.3)	39 (34.8)	10 (41.7)	31 (28.2)	127 (31.9)
mild	66 (49.3)	47 (36.7)	32 (28.6)	8 (33.3)	47 (42.7)	153 (38.4)
severe	25 (18.7)	46 (35.9)	41 (36.6)	6 (25.0)	32 (29.1)	118 (29.6)
Subjective overall health†						
excellent	5 (4.4)	13 (12.7)	7 (6.9)	2 (8.3)	9 (9.4)	27 (7.9)
good	48 (42.5)	47 (46.1)	38 (37.6)	16 (66.7)	41 (42.7)	149 (43.8)
average	47 (41.6)	34 (33.3)	37 (36.6)	6 (25.0)	31 (32.3)	124 (36.5)
poor	9 (8.0)	7 (6.9)	14 (13.9)	0 (0.0)	11 (11.5)	30 (8.8)
very poor	4 (2.9)	1 (1.0)	5 (5.0)	0 (0.0)	4 (4.2)	10 (2.9)
Overall satisfaction†						
excellent	64 (56.6)	64 (62.7)	56 (55.4)	15 (62.5)	53 (55.2)	199 (58.5)
good	42 (37.2)	34 (33.3)	35 (34.7)	9 (37.5)	38 (39.6)	120 (35.3)
satisfactory	5 (4.4)	3 (2.9)	9 (8.9)	0 (0.0)	5 (5.2)	17 (5.0)
poor	1 (0.9)	1 (1.0)	1 (1.0)	0 (0.0)	0 (0.0)	3 (0.9)
very poor	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.3)

*at hospital discharge
†at 30 days.
TYM, Test Your Memory.

5.6 30-day follow-up assessments

5.6.1 mRS at 30 days (III)

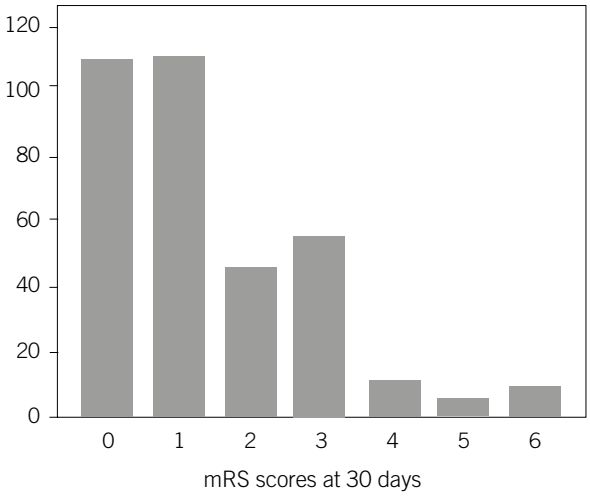
The 30-day mRS scores were available for 350 patients, including those who died during the follow-up (mRS score 6) (Figure 10). The mean and median mRS scores at 30 days were 1.4 (SD 1.5) and 1 (range 0-6), respectively. In univariable analyses, major complications associated with 30-day mRS score ≥3 indicating dependent functional status comprised new or worsened hemiparesis (p=0.001, OR 3.4, CI 1.6-7.4), silent stroke (p=0.003, OR and CI not calculable), and pneumonia (p<0.001, OR 24.5, CI 3.0-202.2). Of individual minor complications, minor infections (p=0.048, OR 2.2, CI 1.0-4.8), and subjective visual disturbances (p=0.002, OR 2.4, CI 1.4-4.4) were associated with high 30-day mRS score (≥3). The associations between 30-day mRS score ≥3 and study outcome measures are in Table 21.

The mRS-score difference from preoperative to 30-day score was available for 349 patients (Figure 11). The median mRS-score difference was 0 (range -4-6). An mRS-score increase (mRS-score difference >0) at 30 days was associated with complication phenotypes hemiparesis (p<0.026, OR 2.3, CI .1-5.1), silent stroke (p=0.013, OR and CI not calculable), pneumonia (p=0.012, OR and CI not calculable), SVD (p=0.027, OR 2.0, CI 1.1-3.6), and minor infection (p=0.043, OR 2.9, CI 1.1-8.2).

Of the 349 patients, 126 (36.1%) patients had mRS-score differences >0 and 57 (16.3%) >1. Almost one-third (31.2%) with good preoperative functional status (mRS score 0-1) and no reported postoperative complications had an mRS-difference >0 at 30 days. The mRS scores did not increase from preoperative to 30 days (mRS-score difference ≤0) in 46.2% of patients in the same subgroup (preoperative mRS 0-1) despite recorded major complications. An increase in mRS score at 30 days (mRS-score difference >0) was associated with the study outcome measures (Table 21).

The mRS scores decreased in 101 (28.9%) and remained unchanged in 122 (35.0%) from hospital discharge to 30 days. Of these 349 patients, 189 had no recorded short-term postoperative complications, yet their mRS scores increased for 45 (23.8%) such patients at 30 days.

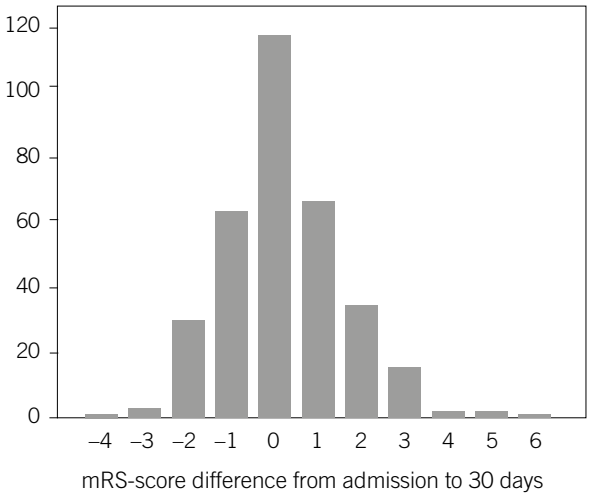
Figure 10. Distribution of mRS scores at 30 days.



mRS, modified Rankin Scale

mRS score at 30 days	Patients (%) N=350
0	110 (31.4)
1	111 (31.7)
2	46 (13.1)
3	56 (16.0)
4	11 (3.1)
5	6 (1.7)
6	10 (2.9)

Figure 11. Distribution of mRS-score differences from preoperative to 30-day scores.



mRS, modified Rankin Scale

mRS-score difference from preoperative to 30-day score	Patients (%) N=349
-4	1 (0.3)
-3	3 (0.9)
-2	31 (8.9)
-1	66 (18.9)
0	122 (35.0)
1	69 (19.8)
2	36 (10.3)
3	16 (4.6)
4	2 (0.6)
5	2 (0.6)
6	1 (0.2)

Table 21. Associations of hospital discharge and 30-day follow-up assessments with study outcome measures. Significant associations in bold, Fisher' Exact test results italicized.

	New CNS deficits				
	p	**OR**	**95% CI**	**sensitivity (%)**	**specificity (%)**
mRS score ≥3 at discharge†	**<0.001**	22.8	10.4-49.9	80.4	84.7
mRS-score difference at discharge >0†	**<0.001**	12.3	5.5-27.3	82.6	72.1
mRS score ≥3 at 30 days‡	**<0.001**	4.7	2.2-9.7	54.5	79.5
mRS-score difference >0 at 30 days‡‡	**0.002**	3.0	1.5-6.4	60.6	66.5
Low overall patient satisfaction**	*0.414*	1.8	0.5-6.5	10.0	94.2
	SI complications				
	p	**OR**	**95% CI**	**sensitivity (%)**	**specificity (%)**
mRS score ≥3 at discharge§	**<0.001**	16.1	6.3-41.3	78.6	81.5
mRS-score difference at discharge >0†	**<0.001**	10.5	3.9-28.3	82.1	69.5
mRS score ≥3 at 30 days‡	**<0.001**	8.2	3.2-20.9	68.2	79.3
mRS-score difference >0 at 30 days‡‡	**<0.001**	5.2	2..0-13.8	72.7	66.4
Low overall patient satisfaction**	*0.079*	3.6	1.0-13.8	17.6	94.4
	Major morbidity				
	p	**OR**	**95% CI**	**sensitivity (%)**	**specificity (%)**
mRS score ≥3 at discharge†	**<0.001**	18.0	9.9-32.8	70.7	88.2
mRS-score difference at discharge >0†	**<0.001**	7.5	4.3-13.2	72.0	74.5
mRS score ≥3 at 30 days‡	**<0.001**	6.0	3.3-11.1	56.4	82.4
mRS-score difference >0 at 30 days‡‡	**<0.001**	3.9	2.1-7.1	63.6	69.0
Low overall patient satisfaction**	*0.054*	2.7	1.0-7.4	12.8	94.9

→

	Overall morbidity				
	p	OR	95% CI	sensitivity (%)	specificity (%)
mRS score ≥3 at discharge§	**<0.001**	6.0	3.5-10.5	38.1	90.8
mRS-score difference at discharge >0†	**<0.001**	5.5	3.5-8.8	53.4	82.9
mRS score ≥3 at 30 days‡	**<0.001**	3.8	2.2-6.4	36.3	61.8
mRS-score difference >0 at 30 days‡‡	**<0.001**	3.3	2.1-5.2	50.6	76.2
Low overall patient satisfaction**	0.215	1.7	0.7-4.3	8.0	95.3

*n=414, †n=405, ‡n=350, ‡‡n=349, **n=340, §n=406

CI, confidence interval; CNS, central nervous system; mRS, modified Rankin Scale; N/A, not applicable; OR, odds ratio; SI, systemic and infectious.

5.6.2 Patient-reported outcomes at 30 days and composite scores of postoperative patient-reported outcomes (V)

A total of 340 (81.3%) patients answered the 30-day structured telephone interview. The 30-day patient-reported outcomes in all study patients, indication subgroups, and the elderly are in Table 20.

Overall health status at 30 days was available for 340 (81.3%) patients, and 88.2% of them reported good overall health. Poor overall health status was associated with dependent functional status (mRS score ≥3) at 30 days (p<0.001, OR 11.5, CI 5.5-23.9).

Poor overall health status at 30 days as associated with new CNS deficits (p=0.004, OR 3.8, CI 1.6-9.2, sensitivity 30.0%, specificity 90.0%) but not with systemic and infectious complications.

Major morbidity was recorded in 13 (32.5%) of 40 patients and overall morbidity in 58 (69.9%) of 83 patients with poor overall health status at 30 days. In univariable analyses, the associations between poor overall health status and both major morbidity (p<0.001, OR 3.7, CI 1.8-8.0, sensitivity 27.7%, specificity 90.8%) and overall morbidity (p=0.002, OR 3.0, CI 1.5-6.0, sensitivity 18.0%, specificity 93.2%) were significant. Both associations lost their significance after multivariable logistic regression analysis.

In elderly patients (age ≥65), a combination of postoperative subjective deterioration in functional status and poor overall health status was recorded in 8 patients, 5 of whom suffered major morbidity

(sensitivity 45.5%, specificity 95.5%), and all of whom suffered overall morbidity (sensitivity 22.2%, specificity 100.0%).

To build a simple, unweighted composite score, i.e. preliminary PROM, we identified 264 (63.2%) patients for whom all three postoperative PROs recorded in this study (postoperative subjective functional status at discharge, postoperative TYM score at discharge, and overall health status at 30 days) were available. Postoperative deterioration in functional status, postoperatively diminished cognitive function, and poor overall health status each yielded one point in the score ranging from 0 to 3. A composite score ≥1 point was associated with major morbidity ($p<0.001$, OR 7.7, CI 2.6-22.8, sensitivity 71.7%, specificity 67.4%) and overall morbidity ($p>0.001$, OR 5.2, CI 3.1-8.8, sensitivity 86.7%, specificity 54.3%). A high composite score (3) was also associated with both major morbidity ($p<0.001$, OR 11.4, CI 3.3-40.3, sensitivity 8.3%, specificity 99.3%) and overall morbidity ($p=0.003$, OR 13.0, CI 1.6-103.1, sensitivity 20.0%, specificity 97.9%).

5.6.3 Patient satisfaction at 30 days (IV)

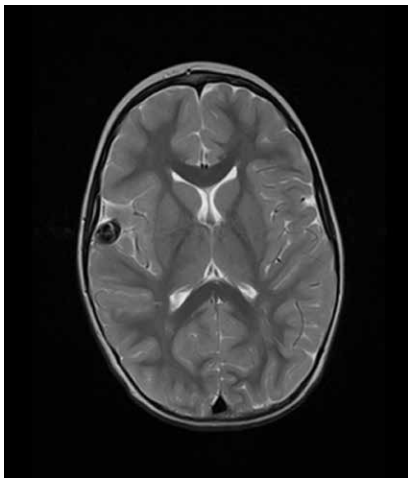
Patient satisfaction was available for 340 (81.3%) patients. Table 20 presents the distribution of patient satisfaction scores in indication subgroups and for elderly patients.

Patient satisfaction in our cohort was high: 93.8% patients rated their overall satisfaction as excellent or good. Poor satisfaction was the response of 3 (0.9%) patients and very poor satisfaction of only 1 (0.3%) (Table 22).

Table 22. Distribution of patient satisfaction scores in all patients and in patients with major and overall morbidity.

Group (patients)	Patient satisfaction, n (%) very poor	poor	satisfactory	good	excellent
All (340)	1 (0.3)	3 (0.9)	17 (5.0)	120 (35.3)	199 (58.5)
Major morbidity (47)	1 (2.1)	1 (2.1)	4 (8.5)	20 (42.6)	21 (44.7)
Overall morbidity (150)	1 (0.7)	3 (2.0)	8 (5.3)	63 (42.0)	75 (50.0)

Altogether 47 patients for whom satisfaction ratings were available experienced major morbidity, however, 42 (89.4%) of them reported high satisfaction (Table 23).



MR image suggesting an aneurysm of the middle cerebral artery.

Of the 19 variables, only 30-day mRS score ≥3 (p<0.001, OR 5.6, CI 2.3-14.0), minor infections (p=0.006, OR 4.9, CI 1.7-13.8), poor subjective overall health status at 30 days (p=0.001, OR 5.5, CI 2.1-14.3), and severe subjective symptoms at 30 days (p=0.038, OR 2.7, CI 1.1-6.6) associated with low overall satisfaction at 30 days. In a subgroup analysis, patients with dependent functional status at 30 days were older (p<0.001) and more likely already functionally dependent preoperatively (p<0.001). Furthermore, they had higher preoperative ASA scores (p=0.02), Helsinki ASA scores (p<0.001), and Charlson comorbidity scores (p=0.002), and longer hospital LOS (p<0.001). This subgroup, in comparison with the whole cohort, also had a higher proportion of malignant tumors (55.4% versus 22.8%, p<.001, OR 4.2, CI 2.5-7.1) and a lower proportion of benign tumors (18.1% versus 34.1%, p=.006, OR 0.4, CI 0.2-0.8).

Table 23. Patient satisfaction in outcome subgroups. Numbers of patients.

Outcome	Patients	Satisfaction available	High overall satisfaction (%)
Unplanned re-CRT or EI	17	13	11 (84.6)
Functionally dependent (mRS score ≥3)			
at hospital discharge	92	56	49 (87.5)
at 30 days	83	73	61 (83.6)
Subjective overall health at 30 days			
poor	40	40	32 (80.0)
good	300	300	287 (95.7)
Subjective symptoms at 30 days			
mild	139	139	130 (93.5)
severe	90	90	80 (88.9)

CRT, craniotomy; EI, endovascular intervention; mRS, modified Rankin Scale.

Low overall satisfaction showed no association with new CNS deficits, systemic and infectious complications, major morbidity, or overall morbidity (Table 21). Patients with low overall satisfaction had a longer hospital LOS than did those with high satisfaction (p=0.001, mean 7.2 versus 5.2 days, median 6.0 versus 4.0 days).

6. DISCUSSION

6.1 Preoperative risk-assessment methods

Evidence for the use of preoperative risk-assessment methods in elective cranial neurosurgery is scarce. Compared to another category of major surgery, cardiac surgery, the number of studies published in neurosurgery is still modest; more than 300 articles on preoperative risk-assessment methods in cardiac surgery appeared in 2011 alone, whereas in Study I the number of relevant neurosurgical studies since 1980 came only to 25. Furthermore, none of the articles were reports on an unselected consecutive series of elective craniotomy patients, only four of the studies were prospective, and cohort sizes were generally small, with less than 100 patients in one-third of the studies included. Those studies with large patient cohorts (>1000 patients) were all retrospective and register-based, thus displaying the inevitable weaknesses associated with such a design: inaccuracy of patient sampling (often selection by CPT codes), lack of detailed preoperative data, and variable but limited rates and types of complications. Neurosurgical centers have yet to widely implement proposed methods of classifying complications after neurosurgical procedures.[156] Direct comparisons and risk calculations were impossible due to considerable differences in assessment methods, study settings, and reporting principles.

Many preoperative risk-assessment scores and models have been proposed for cranial neurosurgery, even ones including intraoperative variables; these scores and models, in a preoperative context, provide merely an estimate based on little more than educated guesswork or statistical means.[102] These scores were excluded from Study I, based on our search protocol. It can be argued whether these can be considered truly preoperative scores, and, at the very least, clinicians should recognize this difference.

Patient characteristics and laboratory measurements

Few preoperatively recorded patient characteristics and laboratory measurements were associated with adverse outcome in Study II. More specifically, no associations were detectable between individual preoperative variables and CNS complications. Furthermore, none of the preoperative patient characteristics or laboratory measure-

ments remained significant predictors for the length of ICU stay or hospital stay after multivariable analyses. Only advanced age and preoperatively elevated CRP were independent predictors of systemic and infectious complications after multivariable logistic regression analyses. (II) Judging by neurological outcome and resource use only, the role of preoperative patient characteristics and especially routine laboratory measurements is questionable; however, non-neurological major complications may still justify the use of such measurements as one risk-assessment tool to improve patient safety.

Reports on the impact of age on outcome of patients with intracranial malignancies have been predominantly negative,[83, 93, 99] but the opposite findings have also emerged.[92] It is noteworthy that interpreting these results may be confounded by the markedly reduced survival reported for elderly patients suffering from malignant intracranial tumors.[157] Study II showed that the rates of major (25.6% versus 28.9%) or overall (45.5% versus 48.9%) morbidity were very similar in all study patients and in elderly patients. In the vascular intracranial surgery group as well, both positive and negative findings exist on the role of advanced age as a predictor of adverse surgical outcome.[85, 96, 101] Our results in Study II imply that overall morbidity was higher in elderly patients than in the overall cohort (51.6% vs 46.4%) and the rate of major morbidity was nearly double that in elderly craniovascular surgery patients (20.7% versus 10.9%), suggesting that age should be taken into consideration when making patient-centered treatment decisions, especially in intracranial vascular patients.

The results of Study II suggest that the predictive value of individual preoperative laboratory measurements is low. This is in keeping with international recommendations discouraging the use of routine screening tests.[63] Only preoperatively elevated CRP retained its significance after multivariable analysis in Study II as an independent predictor of systemic and infectious complications. No previous reports on such association exist. Further studies are necessary to confirm the role of CRP in preoperative risk prediction, but the biological rationale behind the association of preoperatively elevated CRP indicating an acute phase reaction with postoperative systemic and infectious complications is sound.

Low preoperative hemoglobin level was associated with silent stroke but not with any other individual complication or composite morbidity. This may indicate that oxygen delivery to parts of the brain

may be insufficient or compromised in patients with preoperatively low hemoglobin which may be further diluted by perioperative fluid therapy, especially mannitol or hypertonic saline. Contradictory reports on the effect of preoperative anemia on postoperative outcome in elective cranial neurosurgery have recently appeared.[158, 159] Alan et al. detected an association between preoperative anemia and prolonged hospitalization and increased resource use in a large NSQIP database cohort;[158] our results support this finding with a significant association between extended hospital stay and low preoperative Hb. Thus, an active approach to preoperative anemia treatment may be advisable.

ASA score

Study I showed that evidence supports use of the ASA score in predicting overall morbidity[82, 83] and nonsurgical (systemic and infectious)[114, 115] adverse outcomes in elective cranial neurosurgery, especially in patients with intracranial tumors. It should be noted that the criteria for ASA Physical Status Classification scores were not explicitly defined in the articles, and given the considerable interrater variability and national/institutional variation associated with this scale, interpretation of such results should be cautious. Study II results suggest that in an unselected cohort of elective craniotomy patients, the original ASA score could predict neither CNS deficits, systemic or infectious complications, nor resource use (ICU/hospital LOS). Of major complications, high preoperative ASA score predicted only AMI. Thus, evidence for use of the original ASA classification score for preoperative risk assessment of elective craniotomy patients is not compelling.

Helsinki ASA score and composite preoperative risk predictors

Study II validated Helsinki ASA score 4 as an independent predictor of systemic and infectious complications (sensitivity 32%, specificity 85%, PPV 13%, and NPV 95%) as well as of increased resource use after multivariable regression analyses. Our results indicate that the modification provides a tailored risk-assessment scale for the unique patient mix and complications profile in elective cranial neurosurgery.

The Helsinki modification of the ASA Physical Status Classification has received no earlier validation despite having been in clinical use for decades. Compared to the original ASA score, the Helsinki ASA

score seemed more accurate in predicting systemic and infectious complications. The Helsinki ASA score, however, is subject to the same concerns related to interrater variability as the original ASA score. It should be noted that Helsinki ASA scores failed to predict surgical outcomes (new CNS deficits) and thus should probably not serve as the sole risk-assessment method for elective craniotomy patients.

The composite preoperative risk predictor in Study II comprised preoperative Helsinki ASA score 4, preoperative CRP over 3 mg/l, and age 60 years or over. This combination identified almost one in four patients with postoperative systemic and infectious complications. A combination of Helsinki ASA score 4 and age 60 years or over was associated with a nearly 40% increase in ICU LOS and 20% increase in hospital LOS. These simple composites of simple preoperative variables can easily be implemented in clinical practice to support patient-centered decision-making, even in the hectic setting of a preoperative clinic at a tertiary neurosurgical center.

According to these results, the value of the Helsinki ASA may be further enhanced in combination with other predictors. Future studies are needed to develop and validate a tailored risk-assessment score for elective cranial neurosurgery, with Helsinki ASA a possible component for such a composite score.

The mRS score

In our prospective cohort, a preoperatively dependent functional status (mRS score ≥3) predicted both new CNS deficits (sensitivity 19.1%, specificity 90.8%, PPV 20.9%, NPV 89.8%) and systemic and infectious complications in univariable analyses, with slightly lower sensitivity (25.0% versus 32.1%) and a slightly higher PPV (16.3% versus 13.2%), compared to the Helsinki ASA score 4. (Reponen et al., unpublished data)

We recorded preoperative mRS scores primarily to determine the mRS-score differences between preoperative (baseline), hospital discharge, and 30-day follow-up time-points. Preoperative mRS scores have, however, been proposed as a preoperative risk-assessment method for elective craniotomy patients: two studies assessing the applicability of mRS in such a context were included in Study I.[96, 97] Both were retrospective, included patients undergoing intracranial vascular surgery, and had surgery-related outcomes; their results were contradictory.

Our findings (Reponen et al., unpublished data) are in concordance with the results of Study I, in which the KPS, another scale for measuring functional status, received the most support for use as a preoperative risk-assessment scale in elective cranial neurosurgery. The mRS score may prove useful for preoperative risk assessment for postoperative CNS deficits of patients undergoing vascular intracranial surgery, but large prospective studies are necessary to confirm its applicability to such a use.

The Charlson comorbidity score

In our cohort, a high preoperative Charlson comorbidity score (≥3) was associated with systemic and infectious complications. (Reponen et al., unpublished data).

In Study I, three large retrospective studies assessed the applicability of the Charlson Comorbidity score.[99-101] In keeping with our results, evidence supported the use of the Charlson comorbidity score in predicting risk for morbidity and mortality in patients with intracranial tumors (both benign[100] and malignant[99]), and mortality in intracranial vascular surgery patients.[101] In a very recent retrospective study on patients with glioblastoma, the Charlson comorbidity index (a later age-corrected modification of the Charlson comorbidity score) proved beneficial in preoperative patient stratification.[160] The retrospective design and the inclusion of emergency patients complicates comparison of our results with these previous findings, but the Charlson comorbidity score may be an asset in preoperative risk assessment of elective craniotomy patients.

Directions for risk stratification in elective neurosurgery

The Helsinki ASA score had a good AUC (0.81) for mortality, superior to AUCs for all other risk-assessment scores we assessed. In fact, this figure is very similar to the reported AUCs of the Euroscore I (0.77-0.84),[161, 162] and Euroscore II (0.77-0.85),[161-164] for mortality in cardiac surgery patients. The reported AUCs of POSSUM for mortality in gastroenterological surgery patients range from 0.62 to 0.80,[165, 166] and those of P-POSSUM from 0.70 to 0.80.[165, 167] Mortality is too crude a measurement of outcome in modern neurosurgery, but AUCs of the existing scores for all other study outcome measures in our cohort were poor. Our multivariable logistic regression model was able to provide a higher AUC, but still left room for improvement.

It is evident that none of the existing risk-assessment scores fulfills the criteria for a neurosurgery-specific risk-stratification tool. It is surprising that this important topic has received very little attention in neurosurgery, unlike in cardiac surgery, where active research in the field has enabled development of a tailored risk-assessment score widely adopted for clinical use, the EuroSCORE.

6.2 Outcomes and outcome reporting

Currently, no consensus exists on outcome reporting in elective cranial neurosurgery. This was especially evident in Study I, in which outcomes had to be categorized in four broad categories to allow for any summarization of the results. Traditionally, the definition of surgical outcome has been simply new or worsened CNS deficits, but as the focus has turned to patient safety and quality of care, other adverse events, such as systemic and infectious complications, are increasingly included among outcomes. Furthermore, any appropriate outcome measure should be defined by the time-point at which it is measured –if complications attributable primarily to surgical intervention are of interest, the outcomes should be reported soon after surgery, before disease progression, further treatment, or other confounding factors blur the results.

In Studies III, IV, and V, the rate of major morbidity including in-hospital mortality was 18.2%. To obtain as complete complication data as possible we used three data sources: patient-reported questionnaires, study forms, and hospital databases. Even transient hemiparesis was included in major morbidity which can be considered a low percentage for surgery on the most delicate and vital organ, the brain. Morbidity rates in large retrospective database studies range from 15.8% to 23.6%, but direct comparisons with our results are impossible due to data-collection issues and reliability of data. Our results may perhaps be considered as the first prospective benchmarking figures for high-volume neurosurgical centers.

In Study II, the rate of systemic and infectious complications was 6.7%. The only two studies on short-term outcome in an unselected cohort of craniotomy patients reported only systemic and infectious complications. According to Buang and Haspani, surgical-site infections were reported in 7.7% of craniotomy patients, the majority (63.1%) of whom underwent emergency surgery. Kourbeti and coworkers reported a rate of 5.5% for meningitis in a retrospective

cohort comprising both elective and emergency craniotomy patients. We reported a wider range of systemic and infectious complications, but our results are in close agreement with the earlier figures.

In our cohort, the rate of major complications in the subgroup of patients aged ≥65 was 25.0% and of overall complications, 51.6%. These are in agreement with reported morbidity figures of 9% to 54% for elderly patients undergoing intracranial surgery for benign tumors.[75, 78, 84, 168-178] Again, direct comparisons of morbidity rates are, however, impossible due to the extremely variable methodologies and definitions employed across studies.

In our cohort (Studies II-V), the rate of in-hospital mortality was 1.0%, and 30-day mortality was 2.4%. Reported short-term mortality rates for cranial neurosurgery range from 0.0% to 23.0%,[75, 80-83, 86, 88-94, 101, 114, 115] and our low figures support the view that mortality alone is an unsuitable outcome measure for modern elective cranial neurosurgery.

The mRS and outcome

Study III showed that despite significant associations between both high mRS score (≥3) at discharge and mRS-score difference >0 at discharge and major/overall morbidity, the mRS is a poor reflector of short-term outcome; the neurosurgical community could benefit from a more refined outcome-reporting tool.

The mRS is probably the most widely used score for outcome reporting in elective cranial neurosurgery despite its never having received proper validation for such use. This widespread use is highlighted by the most influential studies in cerebrovascular surgery, including the first randomized treatment trial regarding unruptured brain arteriovenous malformations (ARUBA),[18] the International Study of Unruptured Intracranial Aneurysms (ISUIA),[19] and the International Subarachnoid Aneurysm Trial (ISAT).[16, 17, 20]

The mRS score has been conventionally dichotomized at ≥3, indicating a dependent functional status. Due to improvements in neurosurgical care and surgical techniques during the past few decades, however, nowadays only a small percentage of patients suffer from complications sufficiently severe for a postoperative mRS score ≥3. In Study III, one in five cerebrovascular patients and one in four intracranial tumor patients had an mRS score ≥3 at hospital discharge. Of these patients, 35% already had an mRS score ≥3 at baseline (preoperatively), and only 58% had suffered major complica-

tions. Thus, a simple dichotomy seems unable to represent individual complications or even composite outcomes in modern neurosurgery.

The mRS-score differences behave unpredictably with regard to postoperative complications: Nearly one in five patients at hospital discharge and one in four at 30 days had an increased mRS score in the absence of any reported complications. Conversely, no mRS-score increase at hospital discharge was detectable in 28% of those patients with major complications. In the subgroup of patients with good preoperative functional status (mRS score 0-1) and no reported complications, 31% had increased mRS scores at discharge. In the same subgroup (preoperative mRS score 0-1), no increase in mRS score at 30 days was detectable despite major complications in 46% of patients.

Study III showed that after multivariable logistic regression analysis, only new or worsened hemiparesis, silent stroke, and pneumonia, among individual complications, remained significantly associated with an mRS score increase >2 at discharge. Despite these associations, the mRS seems a poor surrogate for overall outcome in elective cranial neurosurgery, and future studies must validate a more reliable tool.

PROs and composite score of PROs

Studying the applicability of validated PROMs in cranial neurosurgery was beyond the scope of this study. Study V results show, however, that even simple PROs or their combinations may be useful for outcome reporting in elective cranial neurosurgery. In Study III, mRS was not an optimal outcome measure after elective craniotomy; in fact patient-reported postoperative deterioration in functional status was more sensitive than dependent functional status (mRS ≥3) for major morbidity (71.4% versus 56.4%) and overall morbidity (58.6% vs 36.6%). In the subgroup of ≥65-year-olds, a growing subgroup in cranial neurosurgery, a simple combination of postoperative deterioration in functional status and poor overall health status at 30 days was highly specific for major (95.5%) and overall morbidity (100.0%).

In a very recent prospective study on a cohort of 191 brain tumor patients, Drewes and coworkers found that retrospective reviewing of patient records, a common method for reporting postoperative adverse events in neurosurgical centers, greatly underestimates the rate of new or worsened neurological deficits, especially cognitive problems, when compared with 30-day PROs.[135] In agreement with

this, Study V results indicate that improving patient safety with the aid of direct patient input need not be complicated, a concern expressed by Varagunam and coworkers.[179] Additional benefits include the absence of observer bias and inter-rater variability associated with conventional scores.[25, 26, 28, 32]

The full potential of PROs is best realized in composites scores or PROMs. Validated PROMs may reduce the impact of diverging methods of outcome assessment in neurosurgical centers around the world. Recent reports by Schiavolin and coworkers show that established PROMs are valid and applicable also in neurosurgical patients.[133, 141] In concordance with this and the findings of Drewer and coworkers,[135] Study V showed that, depending on the chosen cutoff value, even a simple, unweighted composite score of three PROs can improve outcome reporting by providing high sensitivity and specificity for both major and overall morbidity.

6.3 Patient satisfaction

Study IV showed overall patient satisfaction in elective cranial neurosurgery to be high, with 93.8% of patients reporting good or excellent satisfaction in a 30-day follow-up telephone interview. Furthermore, nearly 90% of patients with major complications reported high overall satisfaction, and no association was identifiable between low overall patient satisfaction and postoperative major morbidity. Thus, our results fail to support the perceived association between poor treatment outcome and poor patient satisfaction, and support earlier findings that patient experience and surgical outcome are two separate entities.[146]

Studies have shown that overall patient satisfaction after hospital admission is usually high.[147, 149] In a large retrospective study by Kennedy and coworkers based on University Health System Consortium database data from 171 hospitals, favorable surgical outcomes were not consistently associated with high patient-satisfaction scores.[149] In another retrospective study based on Hospital Consumer Assessment of Healthcare Providers and Systems data from 2 953 US hospitals, Tsai and coworkers found that there need be no trade-off between good-quality care for surgical patients and positive patient experience.[147] Our results are in close agreement with these reports, both in terms of patient satisfaction and quality of care.

Tsai and coworkers reported that hospital stay was shorter in hospitals with the highest patient-satisfaction ratings,[147] whereas Kennedy and coworkers found no such correlation.[149] Our results agree with those of the Tsai group, because in Study IV, low overall patient satisfaction was associated with somewhat longer hospital stay. Causality cannot be confirmed, but Study IV suggests that prolonged hospitalization or factors leading to longer hospital stays may affect overall patient satisfaction. We did not assess changes in patient satisfaction occurring between hospital discharge and 30 postoperative days, but many factors may have an effect on overall patient experience during the recovery period.

An expected association between poor scores in postoperative patient-reported assessments and low overall patient satisfaction emerged in Study IV. Additionally, poor functional status (mRS score ≥3) at 30 days was associated with low overall satisfaction. Interestingly, patients in this subgroup were sicker (higher preoperative ASA scores, Helsinki ASA scores, and Charlson comorbidity scores), were older, had longer hospital stays, and had a higher proportion of malignant tumors and lower proportion of benign tumors than did patients overall who had completed the 30-day follow-up. Plausible explanations are easy to find, but surprisingly no associations between advanced age/comorbidities and low overall satisfaction appeared in the whole cohort. It was beyond the scope of our study further to address any specific underlying factors behind the satisfaction ratings.

The association between minor infections and low overall patient satisfaction in Study IV is somewhat surprising. The underlying mechanism of this association is unclear, as the association lost its significance in the absence of any other complications. Advanced age and longer hospital stay were more prevalent in the subgroup of patients with minor infections, both of which could contribute to patient satisfaction. Furthermore, a low patient-to-nurse ratio (reduced nurse workload) reportedly improves patient satisfaction.[180] Other factors linked with high patient satisfaction comprise increased hospitalization frequencies, higher cost of health care and of prescription drugs, and still more surprisingly, even increased mortality.[181] These observations underline the complexity of factors influencing the patient experience, many of which were beyond the scope of this study.

Only four patients reported poor or very poor overall satisfaction. Of these four, one had an unplanned recraniotomy in the absence of

any other major or minor morbidity. A second patient in this group had a postoperative unplanned endovascular intervention. Due to the low rates of these complications, these are merely case reports, but if unplanned reoperations play a role in patient satisfaction ratings, informing the patients preoperatively of such a rare possibility could improve overall patient satisfaction.

6.4 Limitations of the study

Systematic review

The outcome of patients undergoing emergency neurosurgery is largely dependent on the underlying acute illness.[182] Despite a vigorous attempt to include studies reporting on only elective craniotomy patients, we were unable to fully exclude emergency patients; this was due to incomplete information in the original articles. Study designs, assessment methods, and reporting principals of the chosen studies were highly heterogeneous, making quantitative analyses (meta-analyses) of the results impossible.

Study design

An observational study design does not allow for establishing causality—as opposed to randomized controlled trials (RCTs). Logistic regression was our statistical method where applicable to strengthen the results of our observational study, but the observational design still mandates a cautious interpretation of results.

Cohort size

The cohort size was relatively small. Our cohort was, however, consecutive and unselected, and represents a whole year's case-mix at a tertiary neurosurgical center. Considering the low rate of individual complications in elective cranial neurosurgery, to reach statistical significance cohort size must be substantial. We carried out the study along with normal clinical work at the department without receiving any additional resources.

Selection bias

We were able to enroll only 75.8% of all eligible patients. This therefore may have influenced our results. Older and sicker patients may be less likely to enroll, but without their consent, further analysis of this potential bias was impossible.

Data collection

The patient-reported questionnaires and study forms were complete for 299 (71.5%) patients. A study anesthesiologist filled in all objective data with systematic manual retrieval from hospital records. For statistical analyses, if data were missing, we excluded patients analysis by analysis. Perioperative and in-hospital complications data recording was complete for all patients.

Despite at least three attempts to reach each patient, the response rate for the 30-day telephone interview was only 81.3% (340 patients). To assess the dropout effect, we compared subgroups and conducted post-hoc analyses based on data from hospital patient records obtained at postoperative outpatient-clinic visits. No significant differences were detectable as to the distribution of sex, age, ASA score, Helsinki ASA score, location of craniotomy, indication for surgery, ICU LOS, or hospital LOS. Patients lost to follow-up had a higher rate of major complications and unplanned reoperations and had higher mRS scores preoperatively, both at hospital discharge and at 30 days (Table 24).

Table 24. Characteristics of patients completing the 30-day telephone interview and patients lost to follow-up.

		Telephone-interviewed patients N=340* ‡ (%)	Lost to follow-up (including mortality, ≤30 days) N=78† (%)
Sex	female	215 (63.2)	45 (57.7)
	male	125 (36.8)	33 (42.3)
Age (years)	mean	55.8	58.6
	median	58.0	58.0
ASA score	1	57 (16.8)	10 (12.8)
	2	126 (37.2)	26 (33.3)
	3	139 (40.9)	27 (34.6)
	4	17 (5.0)	12 (19.2)
Helsinki ASA score	1	3 (0.9)	1 (1.3)
	2	83 (24.4)	11 (14.1)
	3	210 (61.8)	41 (52.6)
	4	43 (12.6)	25 (32.1)
Preoperative mRS score	0	90 (26.5)	17 (21.8)
	1	130 (38.3)	28 (35.9)
	2	93 (27.4)	16 (20.5)
	3	19 (5.6)	8 (10.3)
	4	6 (1.8)	7 (9.0)
	5	1 (0.3)	2 (2.6)
Location of craniotomy	Infratentorial	80 (23.5)	24 (30.8)
	Supratentorial	260 (76.5)	54 (69.2)
Indication for surgery	Malignant	101 (29.7)	20 (25.6)
	Benign	102 (30.0)	33 (42.3)
	Vascular	113 (33.2)	25 (32.1)
	Other	24 (7.1)	0 (0.0)
Major complication (excluding reoperations)	yes	40 (11.8)	25 (32.1)
	no	300 (88.2)	53 (67.9)
Unplanned reoperation	yes	12 (3.5)	7 (9.0)
	no	326 (95.9)	71 (91.0)
ICU LOS (days)	mean	1.2	1.9
	median	1.0	1.0
Hospital LOS (days)	mean	5.3	6.7
	median	5.0	5.0

→

Hospital discharge mRS score	0	127 (38.7)	20 (25.6)
	1	83 (25.3)	8 (10.3)
	2	62 (18.9)	14 (17.9)
	3	30 (9.1)	10 (12.8)
	4	23 (7.0)	13 (16.7)
	5	3 (0.9)	9 (11.5)
	6	0 (0.0)	4 (5.1)
30-day mRS	0	110 (32.4)	15 (20.8)
	1	111 (32.6)	13 (18.1)
	2	46 (13.5)	8 (11.1)
	3	56 (16.5)	8 (11.1)
	4	11 (3.2)	11 (15.3)
	5	6 (1.8)	7 (9.7)
	6	0 (0.0)	10 (13.8)

*for ASA score, Helsinki ASA score, preoperative mRS score n=339
‡for hospital discharge mRS score n= 328
†for 30-day mRS scores n=72

ASA, American Society of Anesthesiologists; ICU, intensive care unit; LOS, length of stay; mRS, modified Rankin Scale.

Distribution of mRS score differences (preoperative to 30 days) remained unchanged after the addition of patients lacking a telephone interview but with the 30-day mRS score from outpatient clinic patient records. Results of the post-hoc analyses were similar to the original analyses, indicating that failure to obtain complete follow-up data neither skewed our results nor altered our conclusions.

mRS scores

The inter-rater variability of the mRS is low,[29-31] but such bias cannot be excluded. This shortcoming is, however, probably of minor relevance in terms of conclusions. An anesthesiologist assessed all mRS scores to minimize any surgeon-related bias in reporting outcome. The mRS may be unable to detect changes in functional status if a large proportion of the cohort has high mRS scores at baseline; our cohort had 10.3% of the patients preoperatively functionally dependent (mRS score ≥3).

Methods of measuring postoperative mRS differed at discharge (anesthesiologist's objective assessment) and at 30 days (patient's subjective reporting in a structured telephone interview). Different methods of measurement may have influenced results because sub-

jectivity cannot be excluded in telephone-interview results, but this difference has no obvious implications for their interpretation.

Furthermore, hospital discharge data, including mRS score, was recorded before an unplanned reoperation in 7 patients and after the reoperation in 12. No additional major complications resulted from the reoperations, but we cannot exclude their contribution to the 30-day mRS score. In fact, 30-day mRS was available for 5 of these patients, and for 3 patients (60%) mRS score had increased from hospital discharge to 30 days. Of patients with major complications, 75% had an mRS-score difference >0 at discharge and 66% at 30 days.

Additional confounding factors may have had an impact on the 30-day mRS scores, as it was beyond the scope of our study to record and assess the effect of postoperative rehabilitation or possible health problems leading to admissions in other hospitals during the 30-day follow-up.

Outcome measures

Silent strokes were included among major complications, but according to their definition, they are not expected to have any effect on functional status. Thus, to exclude the possibility of bias in analysis in regard to silent strokes, we repeated the analyses with silent strokes excluded from major complications; the results remained unchanged, indicating that including silent strokes did not skew results.

Categorizing reoperations as complications may be disputed. We chose to do so, as a craniotomy or any other procedure involving the brain potentially affects functional outcome and may lead to additional surgical complications. The indication for a reoperation is often very different from that for the original surgery, however. The most common reasons for a reoperation are to remove a residual lesion or to perform a small reconstructive procedure such as repair of a fistula causing CSF leakage. Thus, many of the reoperations were relatively minor compared to the original surgery.

Additionally, some of the study outcomes were patient-reported. For example, subjective visual disturbances came from the patients' questionnaire at discharge. No clinical neurological-status examination tested for objective findings affecting vision, such as paresis of the oculomotor nerve or defects of the visual field. Thus, the subjective visual disturbances reported may merely reflect minor transient postoperative conditions such as edema of the eyelids or blurriness

of vision due to strong opioid painkillers. The same limitations apply to dysphasia/dysarthria and dysphagia. It is noteworthy, however, that this may have biased the results towards over-reporting outcome events, not underreporting them.

Use of composite outcome measures can draw criticism as an artificial attempt to achieve statistically significant results in a relatively small cohort. The rationale behind this decision was to establish the suitability of mRS as a measurement for overall short-term outcome in elective cranial neurosurgery, not merely an indirect means of measuring the hemiparesis rate.

Length of follow-up

Our follow-up can be considered short. Our aim, however, was to study surgery-related complications and their effect on the mRS. A long follow-up may reflect functional changes attributable to rehabilitation or progression of the underlying disease, such as malignancy.

Patient satisfaction

Patient satisfaction was measured on a five-tier scale from very poor to excellent in the 30-day telephone interview. Patients may be more inclined to report better satisfaction in person, and even over the telephone this "courtesy" bias cannot be excluded. We attempted to minimize this effect by having a study anesthesiologist, not a member of the department's clinical staff who was involved in direct patient care, conducting the interview. Furthermore, events between hospital discharge and the 30-day telephone interview may have contributed to the satisfaction ratings, as all patients who responded to the telephone interview were discharged at the latest on postoperative day 23.

Missing data

We were unable to obtain complete data for all study patients. Altogether 119 (28.5%) patients had incompletely filled-in patient questionnaires and study forms. In-hospital complications, however, were manually retrieved from patient records; thus complete data were available for the entire cohort. Loss to follow-up at 30 days was 68 (16.3%) patients. Post hoc analyses on 30-day mRS scores available for 62 of these patients from patient records indicated no significant bias due to the dropout effect. For each statistical analysis, patients with unavailable data were excluded.

7. CLINICAL IMPLICATIONS AND FUTURE PERSPECTIVES

None of the current preoperative risk-assessment scores in elective cranial neurosurgery receive the support of compelling evidence. It is clear that large, well-designed prospective studies must clarify the role of existing risk-assessment scores, or enable the development of new, neurosurgery-specific preoperative scores. Study II validated the use of the Helsinki ASA score, which proved more accurate in preoperative stratification of elective craniotomy patients than did the original ASA score. The highest value of the Helsinki ASA score was, here, possibly in serving as part of a composite risk predictor for systemic and infectious complications or, in future, serving as a part of a specific risk-prediction score for cranial neurosurgical patients. Furthermore, preoperative functional status (mRS score) and burden of comorbidity (Charlson comorbidity score) also showed potential as tools in preoperative risk assessment, but no score was suitable for use as a sole risk predictor in neurosurgical patients. The value of individual preoperative patient characteristics and laboratory measurements as risk predictors is low, but they may still be useful components of composite risk predictors. Hopefully, our results will encourage the design and execution of international multi-center studies aimed at developing a neurosurgery-specific preoperative risk-assessment score.

The current study provides the first prospective data on complication types and rates in an unselected cohort of adult elective craniotomy patients, and as such may provide tools for preoperative information and patient-centered decision-making. An international consensus on neurosurgical outcome reporting, together with prospective data collection, is crucial not only for benchmarking, but also for meaningful and reliable comparisons between treatment centers. Striving for such a consensus should be a priority for the neurosurgical community, considering the increasing demand for public outcome reporting. The launch of the N²QOD cranial module could be the first step in this direction.

The mRS as an outcome measure in cranial neurosurgery is based not on evidence but on tradition. This study was the first prospective, unselected study that evaluated applicability of the mRS score for

such use. The inconsistency of mRS scores and mRS-score differences with regard to recorded adverse events discourages use of mRS as an outcome measure, regardless of some correlation with new CNS deficits in Study III. In the era of patient-centered health care and patient safety, modern neurosurgery needs a more accurate and reliable tool for outcome reporting, and this remains a topic for future research.

In our cohort, patient questionnaires and study forms provided data which was then manually transferred to electronic form. Electronic data collection is available today in most centers, including ours. It can facilitate prospective data collection for large patient cohorts[183] or even be implemented as a routine protocol for all elective craniotomy patients, as in the N²QOD.[184] Web-based surveys can provide patient-reported data, but technological innovations such as tablet computers should be embraced and harnessed to serve preoperative patient information and patient-reported data collection.

The feasibility of patient satisfaction data does not justify their use as a surrogate for quality of care. The rate of high patient satisfaction is almost similar for all patients and for patients with major postoperative complications. No association between low patient satisfaction and reported complications was detectable in Study IV. Underlying factors contributing to patient experience and satisfaction are complex, and informing patients of the possibility of major complications could further improve patient satisfaction.

Patient-reported outcomes and their composite scores are promising future tools for outcome reporting. In the current study, few individual PROs served to test the feasibility and accuracy of patient-reported data. Study V showed that even individual PROs or their simple combinations can be implemented in clinical practice to provide patient-centered outcome data and improve both patient safety and quality of care. Tailored, neurosurgery-specific PROMs are still lacking, and our results should spark interest in future research in the field. The use of patient-reported variables in preoperative risk assessment in neurosurgery remains an inspiring topic for future research aimed at improving patient safety and quality of care in elective intracranial surgery.

8. CONCLUSIONS

The following conclusions are based on the results of Studies I-V:

1. Evidence as to the applicability of preoperative risk-assessment methods in elective craniotomy patients was scarce. Receiving the most support in the literature was the Karnofsky Performance Score, with some positive results also for the ASA score and Charlson comorbidity score in selected patient populations. None of the existing preoperative scores alone was suitable for predicting overall short-term outcome in elective cranial neurosurgery.

2. Rates of mortality and individual major complications in our cohort were moderately low. No single preoperative variable could reliably predict individual complications. Composite risk predictors and composite outcome measures may best serve in clinical use.

3. The Helsinki ASA score was more accurate and reliable in predicting systemic and infectious complications than was the original ASA score. Combinations, rather than any single preoperative variable or score, seem most suitable for preoperative risk stratification of elective craniotomy patients.

4. The mRS score was a vague outcome measure in elective cranial neurosurgery. Postoperative mRS scores and mRS-score differences failed to reliably reflect the occurrence of postoperative adverse events. PROs were promising tools for patient-centered outcome reporting in elective cranial neurosurgery, and their implementation in clinical practice seems feasible, even in a busy tertiary neurosurgical center. Large prospective studies should validate these findings and guide the development of more suitable outcome measures for elective craniotomy patients.

5. Patient satisfaction after elective cranial neurosurgery was high, even among patients with major complications. Patient dissatisfaction showed no association with a complicated outcome. In quality-of-care comparisons, patient satisfaction should not serve as a proxy for outcome.

9. ACKNOWLEDGEMENTS

This thesis would never have been possible without the support of many important people. I wish to express my deepest gratitude to:

My supervisors, Hanna Tuominen, MD, PhD, and Docent Miikka Korja, for introducing me to the subject of this study. Hanna, thank you for your strenuous work during the study enrollment period, your kind and encouraging words and being there whenever I needed to lighten my heart. Miikka, I admire your expertise and enthusiasm for neurosurgery and science. Thank you for your advice, guidance, lightning-fast replies to any questions at any time of the day or night, and even for pushing me to the limits of my knowledge and ability –no pain, no gain, as they say.

The official reviewers, Professor Risto P. Roine and Docent Minna Niskanen, for the constructive critique which certainly improved this thesis.

The members of my thesis committee, Professor Klaus Olkkola and Docents Tarja Randell and Aki Laakso for showing interest in and support for this research project.

The co-authors of the studies included in this thesis, Docent Tomi Niemi, Marja Silvasti-Lundell, MD, PhD, and Professor Juha Hernesniemi for their expertise and effort in this project.

Docent Markus Skrifvars for Swedish-language editing of the patient questionnaires and expert advice on SPSS® statistical software.

Nurses at the preoperative clinic of the Department of Neurosurgery, Ulla Märsylä, Maria Nevalainen, and Marianne Eliasson for their invaluable help in enrolling the study patients.

The patients, neuroanesthesiologists, neurosurgeons, and nurses of the Department of Neurosurgery at Töölö hospital for making this study possible.

Carol Norris, PhD, for her expert language editing of my thesis and becoming a dear friend during the process.

Docent Anne Vakkuri for her supportive attitude towards my scientific work and enabling study leaves between periods of clinical work. Without this strong encouragement from my clinical superior, my finishing the doctoral training and completing this thesis would never have been possible.

Rita Linko, MD, PhD, and Noora Skants, MD, PhD, for friendly discussions and advice on matters associated with scientific research and even far beyond.

My dear colleagues and nurses in all the places I worked during this research project, especially the anesthesiologists at Peijas hospital, for creating a good working atmosphere and making clinical work enjoyable, even fun at times. A good balance between clinical and scientific work has been imperative for succeeding in this project.

My former superiors at Peijas hospital, Ulla-Maija Lehtonen, MD, and the late Olli Muikku, MD, PhD, for being inspirational role models and believing in me –without such encouraging words I might never have gathered the courage to become a PhD student.

Docent Markku Kuisma and Docent Liisa-Maria Voipio-Pulkki for teaching me important lessons in clinical research during the Out-of-Hospital Hypoglycemia in Helsinki Project in 2001.

My science teachers Mr Bixler and Mr Angeloff back in Santa Barbara, California, for teaching me the basics of scientific thinking and planting the love for science in my heart. This has had a tremendous impact on my path ever since.

My mother Leena, my father Antti, and my sister Johanna for their endless love and support. Starting in my very early years, you have taught me the importance of education and convinced me that with strong will and hard work, any goal no matter how high is achievable.

All my wonderful friends, family members, and choir-mates for the good times, music, laughter, and even occasional tears! You have been irreplaceable in reminding me that life is much more than just medicine or science.

My beloved husband Pade and our sons Emil and Joel, you are my everything. Pade, thank you for your love, companionship, patience, and encouragement during all these years. Thank you for driving thousands of kilometers to Lapland and the Arctic Ocean every year. Those trips have been crucial for my recharging and peace of mind. You have also been an exceptional father and taken the big responsibility of running the daily life of our household to enable me to reach my academic goals, for which I am forever

grateful. Our sons have admirably put up with all the evenings and weekends I have spent on scientific work. The welcome interruptions for bedtime stories and bike rides have kept my priorities straight and put things in the right perspective.

This work has been financially supported by grants from the Helsinki University Hospital Research Fund, The Finnish Society of Anaesthesiologists, and the Finnish Medical Association.

Espoo, October 2015

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12. APPENDICES

Appendix 1. Preoperative patient questionnaire

1. **Basic information:**
   - Name
   - Social security number
   - Date of filling the questionnaire
   - Planned date for operation
   - Age
   - Weight, height
   - Place of residence prior to the operation (home, hospital, assisted residency, health care center, nursing home)

2. **Previous health (no/yes; diagnosis and when diagnosed)**
   - Heart condition
   - Arrhythmias
   - Dyspnea
   - Chronic lung illness
   - Atherosclerosis, carotid artery stenosis, claudication
   - Deep vein thrombosis, pulmonary embolism, thrombogenic condition
   - Stroke, intracranial hemorrhage
   - Cancer
   - Diabetes
   - Epilepsy
   - Other significant illness

3. **How do you rate your general health at the moment (excellent-good-average-poor-very poor), why?**

4. **Smoking**
   - Never
   - Yes, how many cigarettes/day, how many years?
   - Ceased smoking, how many cigarettes/day, how many years, when ceased?

5. **Alcohol consumption during past 7 days**
   - None
   - Moderate: women 1-16 doses, men 1-24 doses
   - Excessive: women over 16 doses, men over 24 doses

6. **How often do you exercise for at least 20 minutes, enough to feel short of breath and break a sweat?**
   - Cannot exercise due to illness or condition
   - Less often than once a week
   - Once a week
   - 2-3 times a week
   - 4 times a week or more

7. **How do you rate your physical fitness at the moment (excellent-good-average-poor-very poor)?**

8. **Can you climb to flights of stairs without stopping?**
   - Yes
   - No, why?

Appendix 2. Postoperative patient questionnaire

1. **Basic information**
   - Name
   - Social security number

2. **Postoperative information**
   - Date of operation
   - Date of hospital discharge (from Department of Neurosurgery)
   - Place of residence after hospital discharge (home, hospital, assisted residency, health care center, nursing home)

3. **Postoperative neurological deficits/symptoms**
   - Short description of symptoms

4. **Postoperative symptoms (No/Yes, what?)**
   - New hemiparesis
   - Postoperative visual impairment
   - Speaking difficulties (Dysphasia, Aphasia)
   - Swallowing difficulties (Dysphagia)
   - Local wound infection, meningitis
   - Other infections
   - Stroke, cerebral ischemia
   - Pneumonia
   - Pulmonary embolism
   - Heart attack

5. **Do you think your functional status has changed after the operation (No/ Yes, how?)**

Appendix 3. 30-day structured telephone interview

1. **Basic information**
   - Patient name
   - Social security number
   - Date of call

2. **Place of residence at the time of the interview (home, hospital, assisted residency, health care center, nursing home)**

3. **30-day mRS31**

4. **How do you rate your general health at the moment (excellent-good-average-poor-very poor)?**

5. **Do you have any persisting postoperative symptoms? (No/Yes, what?) Are they severe/mild?**

6. **Which of the following best describes your overall satisfaction in the neurosurgical care during this hospitalization? Excellent, good, satisfactory, poor, or very poor.**